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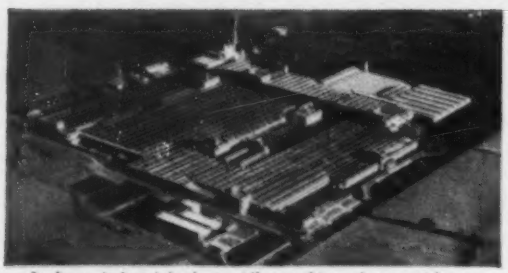

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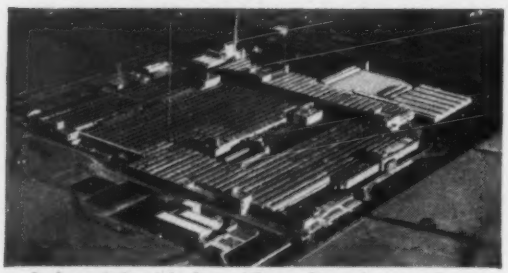

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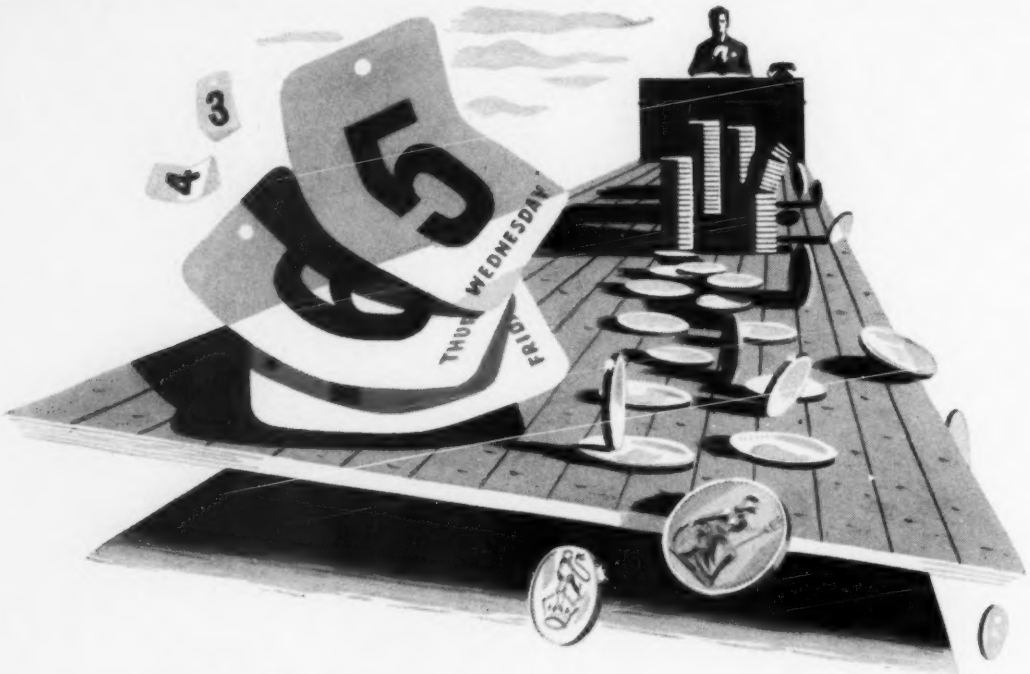

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Brit. J. industr. Med., 1955, **12**, 181.

EMPHYSEMA AND PROTEINURIA IN MEN CASTING COPPER-CADMIUM ALLOYS

BY

J. A. BONNELL

From the Department for Research in Industrial Medicine (Medical Research Council), London Hospital

(RECEIVED FOR PUBLICATION DECEMBER 7, 1954)

Diseases of occupational origin occur as acute or chronic illnesses. The former are usually dramatic and the connexion between symptoms and occupation is obvious. An insidious illness developing over many years and due to long exposure to small quantities of a poisonous substance may long go unrecognized as being of occupational origin.

Since all the recorded cases of chronic cadmium poisoning had occurred among men employed in the alkaline accumulator industry, it was decided to investigate other industries where cadmium is used. This paper describes five cases of chronic cadmium poisoning and reports the results of an investigation of men employed at two factories in England where an alloy of copper and cadmium is manufactured.

Because cadmium increases the wear and durability of copper without reducing significantly its electrical conductivity the alloy is used to replace pure copper for certain purposes. These include post-office telephone wires, high-tension electrical conductor cables, and overhead contact wire for electrically powered omnibuses and trains.

Review of the Literature

Cadmium and its salts have been known to be acutely toxic substances since 1858. The first cases of acute cadmium poisoning were recorded by Sovet in 1858 (quoted by Prodan, 1932) following the inhalation of fine particles of cadmium carbonate which had been used as a silver polish. Numerous reports of acute cadmium poisoning have been published since that time (Frant and Kleeman, 1941 : Huck, 1947).

Stephens (1920) first drew attention to the fact that cadmium might cause chronic ill health. He described the case of a man who had been exposed to small quantities of cadmium in the atmosphere of a zinc spelter works. The symptoms were recurrent bronchitis, loss of weight, and weakness, and the man had been receiving compensation for some time for suspected lead poisoning. At necropsy he was found to have chronic interstitial nephritis and hypertrophy of the heart muscle. The liver was found to contain 0·91 grain of cadmium per pound weight and 0·77 grain of zinc per pound, despite the fact that calamine the zinc ore contained only 0·5 to 1·5% of cadmium and 35 to 40% of zinc. Stephens suggested that the symptoms were due to cadmium and stated that he had seen six similar cases over a period of eight years. Chronic illness due to cadmium was not mentioned in the medical literature again until Mancioli (1940) described chronic rhinitis and pharyngitis in men plating metals with cadmium by an electrolytic process. Mancioli's patients complained of dryness and irritation of the pharynx, a burning sensation in the nose with epistaxis, and were found to have ulcers in the cartilaginous parts of the nose and in the nasopharynx.

In 1942 Nicaud, Lafitte, and Gros investigated a group of workers in an alkaline accumulator factory in France. No details are given about the number of people employed in the factory or the number of people taking part in the investigation. They describe impairment of general health with marked loss of weight, an iron-deficiency anaemia, and severe osteoporosis with pseudo-fractures of the long bones such as are seen in osteomalacia or rickets. They state that chronic bronchitis and emphysema were occasionally seen in their patients but they were of the opinion that the exposure to cadmium was in no way connected with the condition of the lungs. The skeletal changes were cured by administration of calcium and vitamin D, suggesting that nutritional deficiencies, perhaps connected with the Second World War, may have played some part in their production.

Barthélemy and Moline (1946) and Princi (1947) found that men who had been exposed to cadmium for two or more years developed a golden-yellow ring at the alveolar margin of the teeth. Apart from this discoloration of the teeth, Princi found no

evidence of chronic ill health among a group of 20 men who had worked as cadmium smelters for six months to 22 years. The average concentration of cadmium in the atmosphere was found to be as high as 31·30 mg. per cu. m. and the men were found to be excreting between 11 and 125 μg. of cadmium per litre of urine. Princi concluded that exposure to cadmium in these conditions did not cause chronic ill health. Hardy and Skinner (1947) investigated a group of five men who had been exposed to cadmium fume for from four to eight years. These men complained of chronic cough and gastro-intestinal symptoms. Although no definite conclusion could be drawn from such a small group, it was suggested that these symptoms were due to cadmium and that further investigation was necessary to confirm this opinion.

In 1946 frequent complaints of tiredness and shortness of breath among men employed in an alkaline accumulator factory in Sweden led to an investigation by Friberg (1948, 1950). The men made small briquettes of cadmium and iron which compose the negative electrode of the accumulator. During manufacture finely divided cadmium oxide dust passed into the working atmosphere and settled on the floor, machines, and benches and on the clothes, hands, and faces of the workers. Of 58 men investigated, 43 had done this work for more than nine years and complained of symptoms. In order of frequency these were dyspnoea, excessive tiredness, impairment of the sense of smell, cough, and a sensation of dryness of the mouth. On examination the abnormal findings were emphysema for the group as a whole compared with a control group, proteinuria in 35 of the 43, impairment of renal function in nine cases, a raised E.S.R. in 31, and anosmia in 14. The average haemoglobin value in this group was lower than normal. Fifteen men who had worked in the same factory for less than four years were free from symptoms and no abnormality was detected on examination.

The urinary protein could not be demonstrated unequivocally by the boiling test, but a positive result was obtained by testing with trichloracetic acid. Esbach's picric acid test was carried out on 15 cases in which proteinuria had been demonstrated by testing with trichloracetic acid. The Esbach test was negative in 12 cases but an opalescence was observed in seven. The protein was precipitated with full saturation of the urine with ammonium sulphate but not with 50% saturation. The electrophoretic mobility was lower than ordinary albumin at the protein concentration studied, and corresponded more closely to that of alpha-globulin. Electrophoretic analysis was also carried out on five cases after concentrating the urinary protein and this showed three or four components, the largest of which was similar to the protein mentioned above. Examination by ultracentrifuge indicated that the molecular weight of this protein was about 20,000 to 30,000.

Administration of cadmium dust to rabbits by inhalation for two to three hours daily for seven and nine months resulted in the appearance of proteinuria in the majority of the animals. This protein had similar characteristics to the protein found in the urine of the workmen. All the rabbits developed emphysema, and inflammatory foci were found in the kidneys of the majority. In a later paper Friberg (1952) describes animal experiments using radioactive cadmium. It was found that only small amounts of cadmium were excreted in the urine until the proteinuria appeared. There was then a striking increase in the quantity of cadmium excreted, and the concentration of cadmium in the urine was found to bear a direct relationship to the amount of protein in the urine. Friberg suggests that cadmium excreted in the urine is bound to the protein.

Baader investigated a group of 11 workers in an alkaline accumulator factory in Germany. Eight of these, seven men and one woman, were found to have emphysema, proteinuria, and loss of weight. Baader considers that a watery discharge from the nose, which he calls " cadmium snuffles ", is an important early sign. He gives a detailed description of a young man aged 39 in whom this was the first symptom. Eight years later he was so disabled by dyspnoea that he was forced to give up work and he died after three years. Necropsy showed severe emphysema, fatty infiltration of the liver, and toxic nephrosis. The renal lesion is not described in detail, but it is important to note that a protein was excreted in the urine which gave similar reactions to that described by Friberg. Although the man had not been working with cadmium for four years before death, there were large deposits of cadmium in the liver and kidneys.

Friberg and Nyström (1952) report the results of re-examination of the men exposed to cadmium for more than nine years in the alkaline accumulator industry in Sweden. There had been no further exposure to cadmium. Five of these 43 men had died. In two cases death was due to emphysema. Two others had died of coronary thrombosis ; severe renal damage attributed to cadmium was found at necropsy. One man died from acute pancreatitis ; the lungs were found to be emphysematous.

In nine of the remaining 38 men there was evidence to suggest that the disease had progressed.

Increased dyspnoea was complained of by five, proteinuria had developed in four, and in three there was deterioration of renal function assessed by testing the maximum specific gravity of the urine. The symptoms and signs in 25 men were unchanged, whereas in four other men there was a distinct improvement in the performance of tests of respiratory function.

In Friberg's opinion the prognosis for men suffering from emphysema was favourable provided they were removed from exposure to cadmium before the symptoms became severe. Considering that four new cases of proteinuria had occurred and the renal function tests in three men showed greater impairment, Friberg suggests that the renal lesion may eventually become a more important cause of disability than emphysema in many of his cases.

Two fatal cases of emphysema in men casting copper-cadmium alloys were reported by Lane and Campbell (1954). The emphysema developed rapidly over a period of two years without preceding chronic bronchitis or asthma. In one case the diagnosis was confirmed at necropsy. There was widespread emphysema affecting both lungs. In many places the lung substance had been reduced to a coarse spongework but a narrow zone of lung 0·5 to 2 cm. wide under the pleura had been spared. There were therefore no emphysematous bullae on the surface of the lungs. There was little evidence of chronic bronchitis. The cadmium content of the lung was 277 μg./100 g. of tissue, of the kidney 233 μg./100 g., and of the liver 25 μg./100 g.

Manufacture of Copper-Cadmium Alloys

The two factories at which the investigations were made will be referred to as factory A and factory B. Both factories produce alloys of copper containing 0·5 to 1% of cadmium. The details of the process and the types of furnace used in the two factories differ but the method is the same in principle. A master alloy containing up to 50% cadmium is manufactured at both factories by a process which will be described, and known amounts of this alloy are added to molten copper.

Process at Factory A.—The master alloy is made in a coke-fired pit-fire furnace and contains 33⅓% cadmium. Pure cadmium is placed in a crucible which is lowered into the pit fire. When the cadmium is molten, pure copper in the form of copper wire is added. Exhaust ventilation through a flue at the upper half of the pit removes the cadmium fume. As the metals in the crucible become molten they are stirred by the furnaceman to ensure thorough mixing. When the mixing is completed a cover is placed over the crucible before it is removed from the furnace. The molten metal is poured into moulds under exhaust ventilation.

At one time the low-percentage cadmium alloys were produced in this type of furnace. Copper was placed in the crucible and lowered into the pit fire; when the copper was molten the master alloy was added and the mix stirred. Since the stirring was performed manually and there was no exhaust ventilation over the pit the men were exposed to a high concentration of cadmium fume.

The pit-fire furnace is now used only for the manufacture of the master alloy. The present method of manufacture of the low-percentage alloys is by means of an electrically heated, mechanically controlled furnace called a rocker resistor furnace situated in the same workshop. This furnace is barrel shaped and balanced at each end on rockers (Fig. 1). It is heated by a carbon electrode which passes through the centre of the furnace. Bars of pure copper are introduced into the furnace through a door on the long side. The door is closed and the tap-hole is plugged with fireclay. The copper melts in approximately 50 minutes, and at this stage a known amount of the master alloy is added through the door, which is quickly closed. The total charge is 4 cwt. The furnace is rocked to and fro in its long axis by mechanical means to ensure thorough mixing. Since the boiling point of cadmium is 767° C., and the temperature of the molten copper in the furnace is 1000 to 1100° C., a large amount of finely divided cadmium oxide fume is produced each time cadmium is added to molten copper. This can be seen as a dark yellow cloud similar in appearance to nitrous fumes.

Process in Factory B.—The master alloy is manufactured in an oil-fired pit-fire furnace (Fig. 2) and contains 50% cadmium. The process is different from that in factory A in that the copper is placed in the crucible first and when it becomes molten pure cadmium is introduced. Clouds of cadmium fume are produced, and there are no ventilation hoods to remove the fume from the atmosphere. The mix is stirred manually during and after addition of the cadmium and it is then poured into moulds. The workmen wear cotton-wool pads over the nose and mouth.

The low-percentage copper-cadmium alloy is produced in oil-fired tilting furnaces (Fig. 3) in a different workshop. The furnace stands upright and consists of an outer shell lined by fire brick. A crucible containing the copper is placed inside this shell and a space of 2 to 3 in. remains between the crucible and the furnace wall to allow the flames of the burning oil to heat the crucible. When the copper becomes molten the master alloy is added, the mixture is stirred manually, and the alloy is poured into moulds. Hoods with powerful exhaust ventilation are placed over these furnaces by the workmen during casting operations.

The working conditions in both factories are likely to have been very much worse during the Second World War when the black-out interfered with ventilation.

Method of Investigation

In each of the factories there was a small group of men who were working on the manufacture of copper-cadmium at the time of the investigation or who had done so at some time in the past. There was also a larger group of men in each factory who worked in the vicinity of the copper-cadmium furnaces. Control

FIG. 1.—Rocker furnace in factory A.

FIG. 2.—Oil-fired pit-fire furnace in factory B.

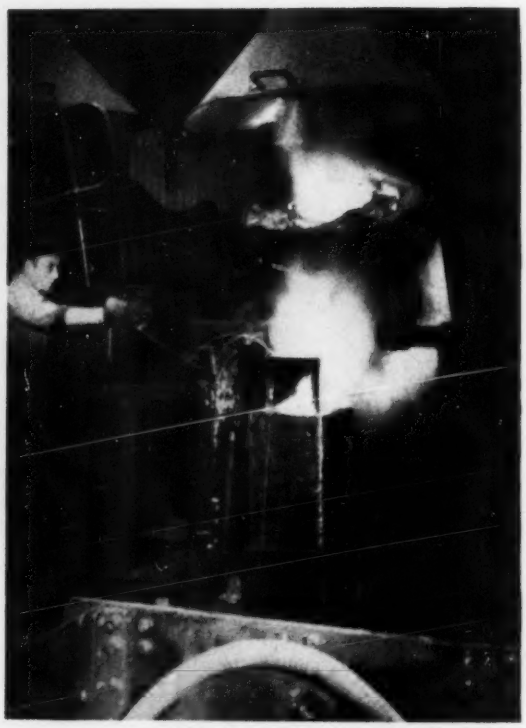

FIG. 3.—Oil-fired tilting furnace in factory B.

groups of men of comparable ages who did similar work but had never at any time been exposed to cadmium were examined at each factory.

The men were asked to volunteer to take part in the survey. Each man was interviewed and a clinical examination made. The occupational history, the past medical history, and the family history were obtained, and specific inquiry was made about suggestive symptoms such as a watery discharge from the nose, loss of sense of smell, yellow discoloration of the teeth, shortness of breath, abdominal pain, and episodes of metal fume fever. At the clinical examination the height, weight, and blood pressure of each man were recorded. Blood was taken by venepuncture for estimation of the haemoglobin concentration, erythrocyte sedimentation rate (Wintrobe), haematocrit, and the plasma proteins. Each man was asked to provide an early morning specimen of urine and 24-hour specimens were obtained from as many of the workmen as possible. They were asked to collect the specimens away from the factory and preferably at week-ends. The early morning specimens of urine were tested for protein, blood, and sugar. In testing for the protein, an equal volume of 25% trichloracetic acid was added to the urine in a test-tube and allowed to stand for 10 to 15 minutes. The urine was tested with 3% sulphosalicylic acid in a similar way. The heat test for protein and Esbach's test were done on all urines which gave a positive reaction with trichloracetic and sulphosalicylic acids. The urine was tested for sugar by Benedict's test and for blood by the benzidine test. The cadmium content of the 24-hour specimens of urine was estimated.

The respiratory function was tested in all the men who attended for examination by measuring the vital capacity, the maximum ventilatory capacity at controlled rates of breathing, and the expiratory fast vital capacity These are tests of the ventilatory capacity of the lungs. From the data obtained by measuring the vital capacity and maximum ventilatory capacities, the swept fractions at given respiratory rates were calculated. These tests and the detailed results are described separately (Kazantzis, 1955). In order to assess the significance of these tests, the results obtained from the study of control groups at each factory are considered as normal for the population investigated. The outer limits of normal represent the mean plus or minus twice the standard deviation for each of the control groups.

All men taking part in the investigation were asked to attend for chest radiographs. At factory A four radiographs of the chest were taken in each case. These were postero-anterior views in deep inspiration and deep expiration, and corresponding left lateral views following the recommendation of Knott and Christie (1951). In fact it was found that the opinion of the radiologist, based on seeing only postero-anterior views, was not influenced by the appearances in the lateral views (Simon, 1953). It was decided therefore to omit taking lateral chest radiographs of the men examined at factory B.

The cadmium content of the working atmosphere was estimated at both factories. The methods employed and the results obtained are discussed in detail by King (1955).

In factory A brass, bronze and copper-cadmium alloys are manufactured in the same workshop. Although only 14 men were casting copper-cadmium, 38 others were engaged in the manufacture of brass and bronze. They had worked in the casting shop for from two to 25 years. Since the workshop was comparatively small (150 ft. by 75 ft.) it was considered that all these men were at risk and they have therefore been included in the exposed group (Group 1A). In addition, six men had worked in this workshop in the past, three manufacturing copper-cadmium and three on the brass furnaces. They have also been included. The total number in Group 1A is therefore 58 men (Table 1). Seven other men working as brass founders in the alloy casting shop refused to take part in the investigation. Early morning specimens of urine were obtained from these men, however, and all were found to be normal. Four men who had worked casting the copper-cadmium alloy were absent from work owing to sickness. They have not been included in Group 1A but they have been investigated in hospital and their case histories are recorded.

TABLE 1

ANALYSIS INTO AGE GROUPS OF MEN EXPOSED TO CADMIUM AND CONTROLS

Age in Years	Factory A		Factory B	
	Exposed Group (1A)	Control Group (CA)	Exposed Group (1B)	Control Group (CB)
25	—	1	1	4
25–34	4	3	11	10
35–44	13	12	15	16
45–54	21	25	9	9
55–64	17	18	5	4
65+	3	1	1	1
Total	58	60	42	44

The control group was made up of 60 men in the same age distribution who volunteered for examination (Group CA, Table 1). They had all worked in different departments of the same factory, but they had never at any time been exposed to cadmium.

At factory B the low-percentage copper-cadmium alloy was manufactured at one end of a large workshop (440 ft. by 180 ft.). There were 15 men employed at the time of the investigation. Four men manufactured the master alloy in a separate department in another part of the works. There were therefore 19 men employed casting copper-cadmium. They had worked with cadmium for from three to 27 years. A further 23 men had been engaged in the manufacture of the alloy for periods varying from 18 months to 28 years, but at the time of the survey were employed in other departments of the factory. These men were included in the exposed group (Group 1B, Table 1) making a total of 42. The control group was made up of 44 men in the same age distribution who had worked in either the brass or the iron foundry for up to 30 years but who had never been exposed to cadmium (Group CB, Table 1).

One hundred and eighty-seven men worked in other sections of the main workshop refining pure copper and

TABLE 2

SUMMARY OF CLINICAL DETAILS OF MEN WITH SIGNS OF CADMIUM POISONING IN FACTORY A

Case No.	Age	Exposure	Symptoms	Clinical Findings	B.P. (mm. Hg)	Hb (g.%)	E.S.R. (Wintrobe mm./hr.)	Urine		Respiratory Function Tests					T.C. (sec.)	Chest Radiograph	Diagnosis
								Early Morning Specimen	Cd in 24-hr. Specimen (μg.)	V.C. (l.)	$S.F._{30}$ (%)	$S.F._{50}$ (%)	$S.F._{70}$ (%)	M.V.C. (l./min.)			
A5	58	18 yr. 1935–53	Dyspnoea 2 yr., cough, loss of weight	Emphysema, liver palpable 2 finger-breadths, soreness of nose	160/110	95 14·1	9	Proteinuria	42	2·78	46·2	31·9	25·6	50	2·08	Emphysema	Emphysema and proteinuria
A6	60	18 yr. 1935–53	Dyspnoea 4 yr., cough 4 yr.	Emphysema, chronic bronchitis, cyanosis	150/100	90 13·3	20	Normal	No specimen received	3·70	65·3	—	—	—	0·73	Emphysema	Emphysema
A7	56	32 yr. 1921–53	Dyspnoea on exertion, no cough	Liver palpable	150/90	85 12·6	9	Proteinuria	104	3·92	78·9	69·1	58·9	162	0·78	Normal	Proteinuria
A8	55	20 yr. 1923–43	Dyspnoea on exertion 4 yr., occasional cough	Emphysema	130/90	105 15·5	10	Proteinuria	58	4·75	47·9	35·4	31·0	103	1·21	Emphysema	Emphysema and proteinuria
A9	56	31 yr. 1920–51	Dyspnoea on exertion	No abnormal clinical signs	—	—	—	Proteinuria	63	—	—	—	—	—	—	—	Proteinuria
A10	42	17 yr. 1936–53	Dyspnoea on exertion 3 yr.	Emphysema, cyanosis	140/90	100 14·8	11	Proteinuria weakly +ve	57	5·5	51·2	38·6	30·8	119	1·11	—	Emphysema and proteinuria
A11	65	40 yr.	Dyspnoea 10 yr., cough and sputum 10 yr.	Emphysema, chronic bronchitis, benign hypertension	210/110	100 14·8	16	Proteinuria	Cd present but not measurable	1·71	69·2	53·4	34·9	42	0·87	Normal	Proteinuria
A12	54	10 yr. 1935–45	Dyspnoea 10 yr., cough 10 yr.	Emphysema, chronic bronchitis	150/100	100 14·8	5	Proteinuria	No Cd	2·39	37·6	30·7	27·3	45	3·13	Emphysema	Emphysema and proteinuria
A13	61	8 yr.	Cough 10 yr., dyspnoea 5 yr.	Emphysema, chronic bronchitis	170/90	95 14·1	16	Normal	No Cd	3·61	49·8	36·3	25·2	64	1·47	Emphysema	Emphysema
Limits of normal obtained by examination of Group CA										2·62	54	44	34	74	0·91		

V.C. = Vital capacity.
$S.F._{30}$ = Swept fraction at 30 respirations per minute.
$S.F._{50}$ = Swept fraction at 50 respirations per minute.
$S.F._{70}$ = Swept fraction at 70 respirations per minute.
M.V.C. = Maximum ventilatory capacity.
T.C. = Time constant of the expiratory fast vital capacity.

TABLE 3

SUMMARY OF CLINICAL DETAILS OF MEN WITH SIGNS OF CADMIUM POISONING IN FACTORY B

Case No.	Age	Exposure	Symptoms	Clinical Findings	B.P. (mm. Hg)	Hb (g.%)	E.S.R. (Westergren mm./hr.)	Urine		Respiratory Function Tests								Chest Radiograph	Diagnosis
								Early Morning Specimen	Cd in 24-hr. Specimen (μg.)	V.C. (l.)	$S.F._{30}$ (%)	$S.F._{70}$ (%)	M.V.C. (l./min.)	T.C. (sec.)	F.R.A (l.)	T.L.V (l.)	R.A./T.L.V. (%)		
B2	49	27 yr. 1926–53	None	None abnormal	130/80	98 14·5	2	Protein +ve	64	5·1	51	33	117	1·33	4·2	7·3	39·7	Emphysema	Emphysema, proteinuria
B3	44	9 yr. 1942–51	Dyspnoea 5 yr., cough, loss of weight	Emphysema, bronchospasm	150/90	90 13·3	15	Protein +ve	1,240	3·89	36	17	47	3·02	5·0	7·4	43·2	Normal	Emphysema, proteinuria
B4	58	22 yr. 1931–53	Dyspnoea 3 yr., cough 2 yr., loss of weight	Emphysema, bronchospasm	150/90	84 12·4	15	Protein +ve	69	2·5	44	27	53	1·38	3·9	6·0	58·3	Emphysema	Emphysema, proteinuria
B5	59	17 yr. 1930–47	Severe dyspnoea 6 mth. onset 5 yr., no cough	Emphysema	140/80	92 13·6	15	Protein +ve	37	3·4	53	37	95	1·50	4·4	7·7	55·1	Emphysema	Emphysema, proteinuria
B6	50	7 yr. 1945–52	Dyspnoea 1 yr., cough 6 mth., loss of weight	Emphysema, bronchospasm, cyanosis, liver palpable 3 fingerbreadths and spleen 2 fingerbreadths	130/70	—	3	Normal	24	2·3	31	16	31	1·50	5·2	7·0	67·1	Emphysema	Emphysema
B7	41	13 yr. 1940–53	None	Normal	116/70	90 13·3	9	Protein +ve	160	3·9	76	50	131	0·48	4·0	7·0	44·3	Normal	Proteinuria
B8	40	17 yr. 1936–53	Slight dyspnoea on exertion	Normal	180/120	—	4	Protein +ve	124	5·3	77	51	189	0·47	2·8	7·1	35·2	Normal	Proteinuria
B9	65	28 yr. 1922–50	None	Normal	150/90	98 14·5	5	Protein +ve	46	3·2	73	52	110	0·59	3·0	5·7	43·8	Normal	Proteinuria
B10	45	7 yr. 1946–53	None	Normal	116/70	96 14·2	10	Protein +ve	375	5·1	65	41	145	0·82	4·5	8·1	39·5	Normal	Proteinuria
Limits of normal obtained by examination of Group CB										3·1	52	31	89	1·1	—	—	—	—	—

V.C. = Vital capacity.
$S.F._{30}$ = Swept fraction at 30 respirations. per minute.
$S.F._{70}$ = Swept fraction at 70 respirations per minute.
M.V.C. = Maximum ventilatory capacity.
T.C. = Time constant of the expiratory fast vital capacity.
F.R.A. = Functional residual air.
T.L.V. = Total lung volume.
R.A./T.L.V. = Residual air/Total lung volume.

casting arsenical copper, bronze and silver bronze, or sorting, inspecting, and cutting the ingots and bars which were cast in the workshop. Of these 187 men, 130 had been employed for more than 12 months and 21 others had at some time in the past been employed in this workshop but at the time of the survey were working in other departments of the factory.

It was estimated that the exposure to cadmium of these 151 men was less than that of men doing similar work in factory A because of the different lay-out in the two factories and the much larger workshop at factory B. They were therefore considered as a separate group in whom the extent of exposure to cadmium was difficult or impossible to assess. Since it was obvious, however, that all were at risk of absorbing some cadmium fume, they were examined. There were no cases in this group in whom the findings were consistent with the diagnosis of chronic cadmium poisoning, and the results of investigation of this group will not be discussed.

Results

In the two factories 100 men who had been exposed to cadmium fume were examined. Of these, nine had emphysema and proteinuria, three had emphysema without proteinuria, and seven had proteinuria without emphysema (Tables 2 and 3). In addition four men at factory A had been forced to give up work because of disabling shortness of breath. They were admitted to hospital for investigation and their case histories are reported separately together with that of one man from factory B who though seriously disabled was still at work at the time of the survey (Table 7). One of the four men from factory A has since died and the necropsy findings are described.

In this investigation independent assessments of the respiratory system were made by clinical and radiological examination and by respiratory function tests. The clinical diagnosis of emphysema was made only when there was a definite history of dyspnoea on effort in a man who had on examination poor chest movement with hyper-resonance on percussion and reduction in the areas of liver and cardiac dullness. The presence or absence of bronchospasm was noted. Heart disease and other lung disease were excluded as far as this is possible by clinical examination alone. The diagnosis of emphysema by clinical examination and radiography is notoriously difficult and there is much disagreement about the specificity of various tests of respiratory function. For the purpose of this investigation the diagnosis of emphysema was made by clinical or radiological examination supported by evidence of impairment of respiratory function assessed as a result of tests referred to above: unless two of these criteria have been satisfied a diagnosis of emphysema has not been made in any man taking part in the survey.

The demonstration of protein in the urine by testing with trichloracetic or sulphosalicylic acids is an objective test which can be confirmed by testing repeated specimens of urine. This type of proteinuria has been taken to indicate absorption of toxic amounts of cadmium and to support the diagnosis of chronic cadmium poisoning.

Factory A.—Nine of the 58 men in Group 1A were considered to be abnormal. Four had emphysema and proteinuria (Table 2). Two had emphysema without proteinuria. Three had proteinuria alone. Case A11 had clinical evidence of emphysema only, respiratory function tests and chest radiographs were normal: for the purpose of this investigation he is not considered as a case of emphysema. Six of these men had worked on the copper-cadmium furnaces for a minimum of 17 years. The other three cases (A11, A12, and A13) had worked in the vicinity of these furnaces for 40, 10, and eight years respectively (Table 4).

TABLE 4
EXPOSURE TO CADMIUM IN YEARS

Years of Exposure	Factory A (Group 1A)	Factory B (Group 1B)
5	4	18
5–9	4 (1)*	11 (3)*
10–14	12	7 (2)*
15–19	12 (3)*	2 (2)*
20+	26 (5)*	4 (3)*

*Numbers of men affected.

One man out of the 60 in Group CA had proteinuria. The protein gave the normal reactions of urinary protein to heat and picric acid and the man was found to have hypertension. No cadmium was found in a 24-hour specimen of urine. There were no cases of emphysema in this group. Chronic bronchitis was diagnosed on clinical examination in four men but respiratory function tests and *x*-ray examination of the chest were normal. In five other men localized areas of emphysema were diagnosed by the radiologist but these men were free of symptoms and the respiratory function tests were normal.

The results of the respiratory function tests are discussed in full by Kazantzis (1955). It was found that there was a significant difference in the performance of the tests between the exposed and control groups (Groups 1A and CA).

The vital capacities (V.C.) and the maximum ventilatory capacities (M.V.C.) are similar in the two groups, but the mean swept fractions at 30, 50 and 70 respirations per minute are significantly lower in Group 1A than in Group CA. The same significant difference is found between these groups for the mean time constant of the expiratory fast vital capacity curve ($p < 0.01$).

TABLE 5

RESULTS OF BLOOD EXAMINATION

Group	Total	Haemoglobin (%)			Haematocrit (c.mm.)			Erythrocyte Sedimentation Rate (Wintrobe, mm./hr.)		
		Mean	S.D.	Range	Mean	S.D.	Range	Mean	S.D.	Range
1A	58	98	±8·0	80–115	43·6	±2·99	37–50	9	±6·64	1–39
CA	60	101	±5·56	90–115	45	±2·87	41–54	6·2	±5·89	1–25
1B	42	90·6	±8·05	74–104	44·9	±3·34	38–55	7·2	±5·16	1–21
CB	44	95·4	±4·31	86–106	45·1	±2·97	35–50	6	±4·11	2–23

The mean and standard deviations of the blood examinations are summarized in Table 5. There was no significant difference in the plasma protein levels.

Eight of the men from Group 1A who had worked on the copper-cadmium furnaces had noticed soreness of the nasal mucous membrane accompanied by a thin watery discharge from the nose, but this ceased shortly after leaving work at the end of the day. None admitted to an impairment of the sense of smell. Because the dental hygiene of these men was so poor it was quite impossible to discover whether the characteristic yellow discoloration of the teeth ascribed to cadmium was present or not.

Seventeen men in Group 1A had worked on the copper-cadmium furnaces and 10 had suffered from metal fume fever while working with cadmium. The majority of the men in Group 1A had experienced similar symptoms at some time following the inhalation of zinc fume during brass casting.

The results of the analysis of the 24-hour specimens of urine are summarized in Table 6. A sample of 200 ml. of urine was wet ashed by boiling with a mixture of concentrated sulphuric and nitric acids. A polarograph was used to measure the quantity of cadmium present.

TABLE 6

CADMIUM EXCRETION IN 24-HOUR SPECIMENS OF URINE

Group	24-Hour Specimens Received	Cadmium	No Cadmium Found	Greater than 30 μg. per Day
1A	44	30	14	15
CA	49	7	42	1
1B	39	32	7	26
CB	40	6	34	2

Twenty-four hour specimens were obtained from 44 of the 58 men in Group 1A. Thirty of these men were excreting cadmium in the urine and 15 of these were excreting more than 30 μg. in 24 hours. Forty-nine of the 60 men in Group CA provided 24-hour specimens. Seven of these men were excreting cadmium in the urine but only one was excreting more than 30 μg. in 24 hours (Table 6).

Factory B.—Ten of the 42 men in Group 1B were considered to be abnormal. Five had emphysema and proteinuria (see Table 3 and Case B1 in Table 7), four had proteinuria alone, and one had emphysema without proteinuria. Case B2 did not complain of symptoms but a diagnosis of emphysema was made on chest radiographs and abnormal respiratory function tests. All 10 men had been exposed to cadmium for over five years (Table 4).

Proteinuria was not demonstrated in any of the 44 men in Group CB. Two men were considered to have *x*-ray changes characteristic of emphysema. Although both were symptom-free, one showed impaired respiratory function.

The results of the respiratory function tests are discussed in detail by Kazantzis (1955). It was found that there was no significant difference between the vital capacities, the maximum ventilatory capacities and the mean swept fractions of the men in the exposed and control groups (Groups 1B and CB). The mean time constant for the expiratory fast vital capacity curve of the men in Group 1B was, however, significantly different from that of the men in Group CB ($0{\cdot}025 > p > 0{\cdot}01$). When the men in Group 1B who had been exposed to cadmium for more than ten years were compared with Group CB, the difference between the mean time constant for the expiratory fast vital capacity curves shows a higher level of significance ($p < 0{\cdot}01$).

The results of estimating the total lung volume and its subdivisions are discussed by Buxton (1955). Thirty-seven men from Group 1B were examined. The men with more than 10 years' exposure showed a significant increase in the mean value of the residual air expressed as a percentage of the total lung volume ($p < 0{\cdot}005$). None of the control group (Group CB) were abnormal. There was no significant difference in the mean value for the total lung volume nor in the efficiency of intrapulmonary mixing between Groups 1B and CB.

As in factory A there were differences in the mean haemoglobin, erythrocyte sedimentation rates, and haematocrit readings in the two groups. The results are given in Table 5, but since these differences

are slight and are the result of single observations, no conclusions can be drawn from them. The plasma protein levels were in close approximation.

Specific inquiries failed to reveal evidence of loss of sense of smell, yellow discoloration of the teeth, or abdominal pains, and none had experienced the symptoms of metal fume fever.

The results of the analysis of the 24-hour specimens of urine are summarized in Table 6. Twenty-four hour specimens were obtained from 39 of the 42 men in Group 1B. Thirty-two of these men were excreting cadmium in the urine and 26 of these were excreting more than 30 μg. in 24 hours. Forty men out of the 44 in Group CB provided 24-hour specimens. Six of these men were excreting cadmium in the urine but only two were excreting more than 30 μg. in the 24 hours. The output of cadmium in the urine from the men in Group 1B was found to be greater than that of the men in Group 1A.

Discussion

Cadmium oxide in the form of dust or fume is extremely toxic. Inhalation of high concentrations gives rise to acute chemical pneumonitis. Stephens (1920), Mancioli (1940), and Hardy and Skinner (1947) suggested that the presence of small amounts of cadmium in the working atmosphere might give rise to chronic poisoning. Friberg (1950), as the result of an investigation of men exposed to cadmium dust in the manufacture of alkaline accumulators in Sweden, described a chronic illness characterized by emphysema and the excretion of a protein of low molecular weight in the urine. Baader (1951) described a similar syndrome in men manufacturing this type of accumulator in Germany.

The results of the present investigation provide further evidence that repeated exposure to cadmium fume does cause chronic ill health. The illness is characterized by progressive shortness of breath and by the excretion in the urine of a protein complex of low molecular weight. Death occurs as the result of pulmonary heart disease or renal failure. In such cases where the occupational history reveals that the patient has been at risk of absorbing cadmium fume or dust the diagnosis of chronic cadmium poisoning is justified.

Tests of the ventilatory capacity of the lungs which were carried out at both factories showed that there was a definite impairment of respiratory function in the groups of men exposed to cadmium when compared with control groups from the same factories.

The clinical examination and chest radiographs of the men who complained of shortness of breath suggested that the disability was due to emphysema. The development of the symptoms and the course of the disease in these cases are unlike the chronic hypertrophic emphysema which follows long-standing chronic bronchitis or bronchial asthma, where cough precedes by many years the onset of dyspnoea on exertion. In only a few of the cases found in this investigation was a history of chronic cough obtained. Dyspnoea usually developed gradually over a period of months or years with the development of a cough in the later stages. In some cases cough and dyspnoea followed immediately after a severe upper respiratory tract infection. Whitfield (1952) reviewed the aetiological factors in 103 cases of emphysema and found that 69 gave a history of long-standing chronic bronchitis or bronchial asthma. Only four cases occurred in his series in which the emphysema had developed without a history of preceding pulmonary symptoms.

In studying the men in Group 1B who had been exposed to cadmium for more than 10 years. Buxton found that the volume of the residual air and the residual air expressed as a percentage of the total lung volume were both significantly increased. This is often found in emphysema, When, however, the mean value for the total lung volume of this group was compared with that of the control group (Group CB) it was found to be unaltered and the range was not increased. Furthermore, the mixing coefficients were within normal limits. These results suggest that there are certain differences between the emphysema which develops in men exposed to cadmium fume and the chronic hypertrophic emphysema which follows long-standing chronic bronchitis. In the latter the intrapulmonary mixing coefficient is low and the total lung volume is increased.

Lane and Campbell (1954) describe the necropsy findings in a man who worked on the copper-cadmium furnaces at factory B. In their case not only were there no emphysematous bullae at the periphery of the lungs but there was a narrow zone of normal lung tissue under the pleura and chronic bronchitis was neither widespread nor severe. Thus, the mode of onset, the results of respiratory function tests, and the findings at necropsy in one case support the view that the emphysema which develops in men who have been exposed to cadmium fume is different from the chronic hypertrophic emphysema which follows upon chronic bronchitis. Chronic bronchitis, however, may develop as a complication in men whose lungs have already been damaged by the repeated inhalation of cadmium.

Knowledge of the pathological process and the morbid anatomy of chronic cadmium poisoning

will be fully understood only when more cases have been studied at necropsy.

Friberg (1950) found that the majority of men who had been exposed to cadmium oxide dust in the alkaline accumulator industry for more than eight years excreted a protein in the urine which did not give the usual reactions of urinary protein or Bence-Jones protein. Electrophoretic analysis and examination with the ultracentrifuge suggested that this protein was a globulin and that the molecular weight was in the region of 20,000 to 30,000.

In the present investigation 19 men were found to have proteinuria which gave reactions to routine clinical laboratory tests similar to those of the protein described by Friberg. The boiling test for protein was unreliable; in some cases it was negative and in others a slight cloudiness only was apparent. It was found that non-specific protein precipitants such as 25% trichloracetic acid and 3% sulphosalicylic acid gave positive reactions when the boiling test was negative or doubtful. Esbach's picric acid reagent produced a general cloudiness on standing but the protein did not settle in the tube so that quantitative determinations by this method were unreliable. Kekwick (1955) describes the results of physico-chemical examination of the serum and of the protein excreted in the urine of four men chosen at random from these 19 cases. The electrophoretic analyses of the sera showed that the proportion of gamma globulin was abnormally high in two cases and that the alpha globulin proportion was slightly above the normal value in all four cases (Kekwick, Table). There did not appear to be a uniformly consistent deviation from the normal which could be attributed unequivocally to cadmium poisoning. Except for one case the electrophoretic pattern of the urinary proteins was similar to those shown in Fig. 1A (Kekwick), where there appears to be a large number of ill-defined components covering a mobility range similar to that of the serum proteins. In Case A3 (Fig. 1B, Kekwick), four relatively well defined components were present but the total protein content of the urine was much higher than in the other cases. In the ultracentrifuge the urinary proteins sedimented as a single component in all four cases. The sedimentation constants correspond with a molecular weight in the range 20,000 to 30,000. Further work is necessary to determine the nature of this protein and to establish whether it is excreted in some form linked to cadmium.

Baader (1952), reporting the case of a man who died as the result of chronic cadmium poisoning, describes the kidney lesion as a toxic nephrosis. In the fatal case reported in this paper (Case A1), the man died as the result of chronic renal failure. He was under observation for 18 months before death and tests confirmed that the proteinuria was quite unlike that usually associated with chronic glomerulonephritis. The electrophoretic pattern of the protein was non-specific but it was found to have a low molecular weight (Kekwick). On microscopic examination of the kidneys Professor Dorothy Russell was of the opinion that the changes were indistinguishable from the nephritis repens of Bright's disease. Further evidence that cadmium causes renal damage is provided by Friberg and Nyström (1952) who re-examined the workmen in the alkaline accumulator industry after five years.

There was no evidence to suggest that these men had any impaired sense of smell, but this may be due to the fact that they were exposed to cadmium oxide fume whereas men who were found to have this complaint in the alkaline accumulator industry were exposed to cadmium oxide dust.

The importance of the presence of cadmium in the urine, except as a confirmation of absorption, is difficult to assess. The quantity of cadmium excreted does not appear to bear any relationship to the severity of poisoning. Workmen exposed to cadmium excreted between 0 and 800 μg. of cadmium per day. Forty-one were excreting more than 30 μg. daily. It was of interest that men who had ceased to work with cadmium for as long as 10 years were still excreting measurable quantities of cadmium in the urine.

All 19 men showing symptoms or signs of chronic cadmium poisoning in this investigation had been exposed to cadmium for more than five years and 13 had been exposed for more than 15 years. Of six men in Group 1B who had worked on the copper-cadmium furnaces for more than 15 years, five were affected (Table 4). All the cases of chronic cadmium poisoning described by Friberg (1950) had more than eight years' exposure to cadmium oxide dust.

The maximum allowable concentration of cadmium in the working atmosphere has been set at 100 μg. per cu. m. (American Conference of Governmental Industrial Hygienists, 1954). In this investigation the average concentration of cadmium in the atmosphere of the workshop over 12-hour periods did not exceed 270 μg. per cu. m. in either factory, but for periods of 15 to 20 minutes every hour during casting the concentration was much higher (King, 1955). These findings are unlikely to be a true reflexion of the working conditions at the time when the majority of the men affected started work. To comply with black-out regulations during the Second World War all windows and doors had to

be closed and covered at night, and the natural ventilation of the workshops was consequently reduced. The average concentration of cadmium in the atmosphere is likely to have been much greater than that found in this investigation. Because there was no evidence in the medical literature to suggest that cadmium could produce chronic ill health, few precautions were taken to remove cadmium from the atmosphere during the war years and in the immediate post-war period. All the men who were affected had worked for at least seven years. Since 1948 conditions have been greatly improved and precautionary measures have been introduced in each factory.

Summary

The results are reported of an investigation of men employed at two factories in England where alloys of copper and cadmium are manufactured.

Five cases of chronic cadmium poisoning including the necropsy findings in one fatal case are described. The findings in a further 18 cases are summarized.

Chronic cadmium poisoning is characterized by (*a*) the development of emphysema, in which there is some evidence to suggest that the emphysema is not the same as chronic hypertrophic emphysema which follows chronic bronchitis or bronchial asthma ; (*b*) renal disease which is accompanied by the excretion in the urine of a protein with a molecular weight of 20,000 to 30,000. The urinary protein does not give the same reactions to routine clinical laboratory tests as the proteinuria which occurs in glomerulonephritis, cardiovascular-renal disease, or Bence-Jones protein.

Emphysema and proteinuria may both be present or may occur separately in a particular case.

In the fatal case death was due to chronic renal failure.

Twenty-four hour specimens of urine were obtained from 83 men exposed to cadmium. Cadmium was present in 62 cases and 41 of these were excreting more than 30 μg. per day.

The cadmium concentration of the working atmosphere was estimated under the present working conditions and the significance of these findings in relation to conditions of work in time of war are discussed.

I am indebted to the management of the two factories concerned, particularly the medical and personnel departments without whose wholehearted cooperation the investigation could never have been made.

I wish to thank Dr. Donald Hunter and Dr. P. L. Bidstrup for their encouragement and helpful criticism ; Professor J. L. D'Silva for his ready assistance in arranging for the respiratory function tests to be carried out ; Dr. George Simon for reading the chest radiographs ; Professor Dorothy Russell for the pathological and histological report on Case A1 ; Professor Melville Arnott for permission to publish Case A4 ; Professor R. V. Christie for his opinion and arranging further respiratory function tests on Cases B1 and B3 ; Miss Jean Peal and Messrs. D. Lawford, E. Palmer, and T. Emerson, for valuable technical assistance. I should also like to thank Dr. D. G. Harvey, Dr. E. H. Evison, and Dr. G. Webster.

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APPENDIX I

Case Histories

Case No. A1 (L.H. Record No. 12133/53).—This was a man aged 54 years suffering from chronic renal failure without hypertension and a moderate degree of emphysema. On repeated examination of the urine, the only protein demonstrated was one of low molecular weight which differed from the proteins usually found in the urine in chronic renal disease (Kekwick, Fig. 1). He served in the Armed Forces until 1920 and from 1920 to 1952 he had worked casting an alloy of copper and cadmium. He had also cast brass and bronze during this time. He had always worked on the pit-fire furnace and for the greater part of this time was responsible for casting the "master alloy" containing 33% cadmium with copper. He had not worked since November, 1952.

He was admitted to the North Staffordshire Royal Infirmary in March, 1953, and transferred to the London Hospital in April, 1953, for further investigation. He was readmitted in uraemic coma on May 20, 1954, and died on May 22.

He was perfectly well until 1948 when he began to get attacks of unproductive cough. These attacks persisted until he stopped work in November, 1952. For 18 months before admission to hospital he had been short

TABLE 7

SUMMARY OF CLINICAL DETAILS OF MEN SERIOUSLY DISABLED BY CADMIUM POISONING

Case	Date	Hb (g. %)	E.S.R. (Westergren mm./hr.)	Renal Function Tests		Urine		Respiratory Function Tests					Chest Radiograph	Other Data
				B. Urea (mg./100 ml.)	Urea Concentration Test (maximum urine urea mg./100 ml.)	Midstream Specimen	Cd in 24 Hours (μg.)	V.C. (l.)	$S.F._{.30}$ (%)	$S.F._{.70}$ (%)	M.V.C. (l./min.)	T.C. (sec.)		
A1	8. 4.53	41 6·1	80	144	900	Proteinuria	30–40	—	—	—	—	—	Normal	Liver function tests normal, normoblastic bone marrow, plasma proteins, see Table 1, Kekwick
	9.11.53	30	25	141	—	,,	—	2·83	58	43	74	0·79	Emphysema	
	20. 5.54	26	—	454	—	,,	—	—	—	—	—	—	—	Died on 22.5.54
A2	3. 2.53	111 16·5	50	39	1800	,,	290–980	2·46	42	24	42	2·39	Emphysema	Liver function tests normal, plasma proteins, 6·45. (albumin 3·22 g. per 100 ml., globulin 3·23 g. per 100 ml.), urea clearance test, 62% 1 hr. P.S.P. excretion, 33·5% 1 hr.
A3	26.10.53	94	34	42	2500	Proteinuria 0·55 g./100 ml.	46	2·45	30	17	31	2·45	Emphysema	—
A4	18. 3.52	104	3	—	—	No protein	112	—	—	—	—	—	Emphysema	8.4.52. The results of cardiac catheterization were compatible with emphysema
	6. 8.53	110	3	38	2400	No protein	—	2·08	30	17	25	4·0	Emphysema	
B1	25. 3.54	103	2	45	1920	Proteinuria	59	2·8	31	17	32	3·27	Emphysema	The mixing efficiency, pulmonary diffusing capacity (carbon monoxide technique), and intra - oesophageal pressure studies were carried out at St. Bartholomew's Hospital, London. It was concluded that the disability was due to a moderate degree of emphysema associated with bronchospasm

of breath on exertion. This was accompanied by a dull, aching pain in the left upper chest which was relieved by resting. There was no past history of haematuria or renal disease.

On examination in April, 1953, there was pallor of the skin and mucous membranes but no obvious loss of weight. There was a pronounced uraemic odour in the breath. He was not dyspnoeic at rest. There was no clinical evidence of cardiac enlargement, but a soft systolic murmur was audible in all areas. The blood pressure was 165/85 mm. Hg on admission to hospital but later fell to and remained at 130/60 mm. Hg. The chest was barrel-shaped and there was increased resonance on percussion with diminution in the area of liver dullness. The breath sounds were vesicular and there were no adventitious sounds. There was no abnormality on examination of the abdomen and the central nervous system.

He was treated with a low-protein diet and unrestricted fluids, but on discharge from hospital his condition was unchanged.

He was readmitted to hospital on November 9, 1953, owing to increasing pallor, shortness of breath, and oedema.

There were purpuric spots scattered over the chest and legs with marked oedema of the legs and back.

He was treated by rest in bed, digitalis folia gr. 1 twice daily, abundant fluids by mouth, and a low-protein diet. He was cautiously transfused with the packed cells of 14 pints of blood over six weeks with marked improvement. On discharge from hospital, haemoglobin was 96% and the blood urea was 165 mg./100 ml.

He was readmitted on May 20, 1954. He had become increasingly drowsy and breathless on exertion for several weeks. On examination he was very pale and almost comatose. There were purpuric haemorrhages of the buccal mucous membranes. There was a pericardial friction rub and the blood pressure was 140/100 mm. Hg.

Haemoglobin was 26% (3·8 g.%) and the blood urea was 454 mg. per 100 ml.

The results of laboratory and other investigations are summarized in Table 7.

Necropsy Findings.—The lungs were oedematous and there was a moderate, diffuse emphysema, with occasional bullae measuring up to 2 by 1 cm. There was a small area, 6 by 3 cm., of focal bronchiectasis in the inferior and posteromedial aspect of the left lung.

There was a sero-fibrinous pericarditis, the pericardial sac containing about 30 ml. of free fluid. The left ventricle was hypertrophied and slightly dilated, and there was slight general atheroma with a few flecks in the main pulmonary arteries.

There was considerable reduction in the size of the kidneys, which weighed only 99 g. The subcapsular surfaces were smooth and grey. The renal cortex was narrow and had an indistinct pattern but contained a few small cysts measuring up to 0·3 cm. in diameter.

The liver was pale and oedematous, weighing 1,829 g. It showed a strong iron reaction as did the otherwise normal spleen. There was mucous catarrh of the stomach and intestines. The endocrine glands and brain were normal.

There was osteoporosis of the sternum, ribs, femora, right radius and ulna, and thinning of the vault of the skull. The sternum and ribs were easily cut with a knife. The sternal marrow was partly adipose and there were islands of bright pink marrow in the upper 8 cm. of the shaft of the right femur. The corticalis of the femur was white and dense.

CADMIUM IN TISSUES

Tissue	Wet Weight (g.)	Cd in Sample (mg.)	Cd /100 g. Tissue (mg.)
Muscle	50	0·560	1·120
Lung	125	2·53	2·024
Kidney	20	1·23	6·15
Liver	75	24·76	33·01
Spleen	50	1·94	3·88
Small intestine	150	1·15	0·764
Rib	40	0·290	0·725
Long bone	30	0·150	0·50

Both lobes of the left lung and the lower lobe of the right lung showed great but uneven emphysema. The subpleural zone was not spared. There was moderate anthracosis, and occasional dust-macrophages occupied alveolar spaces. There was no fibrosis and no inflammatory interstitial infiltration apart from a few foci of lymphocytes which were usually adjacent to arteries. In the less emphysematous parts there was extensive oedematous exudate in the alveolar spaces with early stages of purulent bronchopneumonia. The bronchioles elsewhere showed mucous catarrh only. No structural changes were present in the arteries and arterioles.

The pericardium, in sections from both ventricles, bore a few superficial deposits of fibrin. There was oedema of the epicardium which was sparsely infiltrated with polymorphonuclear leucocytes and round cells. This infiltration extended into the adjacent intermuscular septa. The muscle fibres of the right ventricle were slightly hypertrophied, and in the left ventricle this change was more pronounced. In the latter a few small foci of fibrosis were found in the deeper parts of the myocardium. The associated blood-vessels were normal.

The cortex of the kidneys was uniformly reduced in depth and was diffusely affected by interstitial fibrosis. Many of the glomeruli had undergone ischaemic atrophy in association with fatty-hyaline degeneration of the smaller arterioles. Residual glomeruli frequently appeared unchanged, but some showed degenerative changes in the tuft best demonstrated by the presence of focal sudanophil deposits in the lobules. In such glomeruli there were sometimes adhesions between the tuft and Bowman's capsule. This degenerative change was evidently of a progressive character because a good many glomeruli could be identified in advanced stages of non-ischaemic atrophy, that is, a shrinkage with complete loss of cells in the tuft without the hyaline collagenous thickening of Bowman's capsule that characterizes ischaemic atrophy.

The tubules were often grossly atrophied, containing hyaline casts. Other tubules were dilated, containing brightly eosinophil granular casts mingled with leucocytes, or aggregates of leucocytes alone. In such tubules the epithelium was flattened and the distinctive features of the proximal and distal parts of the nephron were lost. Casts were very conspicuous in the collecting tubules of the medulla. The density of the collagen fibres in the interstitial tissue was variable. Where this was least dense the tissue was more cellular and contained spindle fibroblasts. There was a good deal of lymphocytic infiltration, especially beneath the capsule and near the junction of cortex and medulla. No sudanophil material was present either in the tubules or interstitial tissue.

In addition to fatty-hyaline changes in the arterioles, the larger arteries showed moderate hypertrophy.

Sections from the sternum, a rib, and the right femur showed advanced osteoporosis. The marrow in all was partly adipose ; haemopoiesis appeared normal.

No structural changes were present in the liver. The Kupffer cells contained free iron-pigment. Only slight fatty change affected the parenchyma and this was of irregular distribution.

The pulp of the spleen was congested and considerable amounts of free iron-pigment occupied groups of macrophages.

The pituitary, parathyroids, adrenal, and thyroid were normal, apart from discrete colloidal adenomata in the last-mentioned.

In the testis there was diffuse atrophy of the seminiferous tubules without inflammatory infiltration. In a few foci atrophy was complete.

No abnormality was found in sections of the hypothalamus, basal ganglia, and cerebellum.

Case No. A2 (L.H. Record No. 3919/53).—A man aged 52 years suffered from severe emphysema with slight impairment of renal function. The characteristic protein was present in the urine. He had worked all his life in the non-ferrous metal industry but from 1937 to 1950 he had been casting an alloy of copper and cadmium, the first three years on the pit-fire furnace and the latter 10 years on the rocker resistor furnace. He was admitted to the London Hospital in February, 1953.

He was quite well until 1945. Dyspnoea developed at this time and by 1949 he was unable to do his usual job. There was no wheezing and no seasonal variation of the dyspnoea. He developed a persistent cough in

1949 producing 2 to 3 oz. sputum daily. In 1950 he was given a light job in another department in the factory and since 1951 he has been unable to work at all. He had lost 2 to 3 st. in weight since 1948, appetite was poor, and he complained of slight epigastric pain.

On examination in February, 1953, there was obvious muscle wasting and he was short of breath on the slightest exertion. The cardiovascular system was normal with a blood pressure of 115/75 mm. Hg. The chest was barrel-shaped and chest movements were much diminished. There was increased resonance on percussion of the chest and cardiac and liver dullness could not be elicited. Heart sounds were distant, the breath sounds were vesicular, and scattered rhonchi were audible over both lungs. The spleen was palpable two fingerbreadths below the left costal margin and the liver edge was just palpable below the right costal margin. There was no abnormality of the nervous system.

The results of laboratory and other investigations are summarized in Table 7.

Case No. A3 (L.H. Record No. 38128/53).—A man aged 58 years suffered from severe emphysema. The characteristic protein was present in the urine. Except for service in the army in 1914–18 he had always worked in the same factory, and from 1935 to 1946 had been casting alloys of copper and cadmium. He had been employed on the rocker resistor furnace during the whole of this time. In 1946 he was forced to take a light job and since that time he has been unable to resume his former occupation.

He was admitted to the London Hospital in October, 1953. He was quite well until 1943 when he developed cough and dyspnoea. The cough has persisted and the dyspnoea has gradually become more severe. At the present time he can walk only 20 to 30 yards. During the past four years he has complained of a sensation of tightness in the left upper chest which is relieved by rest. Since 1940 he has noticed a clear, watery discharge from the nose which is unrelated to upper respiratory tract infection. He has lost almost 2 st. in weight since 1946.

On examination in October, 1953, there was evidence of marked loss of weight, and he was short of breath on slight exertion. There was cyanosis of the lips. The heart was not enlarged clinically, pulse was regular at 90 beats per minute, and the blood pressure was 130/75 mm. Hg. The chest was barrel shaped with increased resonance on percussion and diminution of cardiac and liver dullness. Breath sounds were present over both lungs, with many high-pitched expiratory rhonchi and basal crepitations.

The results of laboratory and other investigations are summarized in Table 7.

Case No. A4 (L.H. Record No. 25498/53).—A man aged 49 years suffered from severe emphysema. He had always worked at the same factory except for four years in the Potteries where he had been employed grinding clay in a water mill. From 1935 to 1947 he was casting copper alloys : bronze and brass only from 1935 to 1939 but from 1939 to 1947 he had been employed on the pit-fire furnace casting the copper-cadmium master alloy. Because of his symptoms he changed to a light job in 1947 and has been unable to work since 1950. He was admitted to the Queen Elizabeth Hospital, Birmingham, in March, 1952, and to the London Hospital in August, 1953.

He suffered from a cough from 1942 but there was no disability until 1947, when he noticed that he was getting short of breath on exertion. The dyspnoea became steadily more severe and at present he is able to walk only 25 to 30 yards on level ground. There has been marked loss of weight, amounting to 3 st. in six years. He has suffered from nasal catarrh with a clear mucous discharge since 1940, and he complains of right subcostal pain aggravated by exercise since 1947.

On examination in March, 1952, he was thin, orthopnoeic, and the lips were cyanosed. The cardiovascular system was normal with a blood pressure of 140/90 mm. Hg. The cardiac apex was not palpable and the heart sounds were faint. The chest was barrel shaped with gross diminution of movement on respiration. The expansion of the chest was ½ in. There was increased resonance on percussion of the chest, and cardiac and liver dullness were absent. The breath sounds were audible in both lungs with generalized, high-pitched expiratory rhonchi. Neither the liver nor the spleen was palpable and palpation of the abdomen showed no abnormality. There was no oedema of the ankles.

The results of laboratory and other investigations are summarized in Table 7.

Case No. B1 (L.H. Record No. 9954/54).—This man aged 52 years was suffering from emphysema with slight impairment of renal function. The characteristic protein was present in the urine. He had worked from 1930 to 1940 casting alloys of copper and cadmium in a pit furnace.

He was admitted to the London Hospital in March, 1954.

He first noticed dyspnoea on exertion in 1939. He changed his job in 1940 on the advice of his doctor and since this time has worked in another department of the factory. Since 1951 he has become increasingly dyspnoeic on exertion and he has lost 2½ st. in weight. He has complained of epigastric pain, relieved by alkaline powders, since 1950.

On examination in March, 1954, there was evidence of marked loss of weight and he was dyspnoeic at rest. There was no cyanosis, finger clubbing, or pallor. The cardiovascular system was normal and the blood pressure was 140/90 mm. Hg. The thoracic cage was fixed in inspiration, movement was poor, and there was hyper-resonance on percussion of the chest with absent cardiac and liver dullness. Air entry was good, breath sounds were vesicular with occasional scattered rhonchi.

The results of laboratory and other investigations are summarized in Table 7.

APPENDIX II

Physico-chemical Examination of the Serum and Urine Proteins in Some Cases of Cadmium Poisoning

BY

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Although Friberg (1950) in his monograph on cadmium poisoning gives some data concerning the electrophoretic and ultracentrifugal behaviour of the serum and urine proteins from such cases, the provision of further data in connexion with the present series described by Bonnell (1955) seemed advantageous.

Methods

Treatment of Urine and Serum.—In general the concentration of protein in the urine was too low to permit a satisfactory physico-chemical examination to be made in the usual manner, that is, after simple dialysis to equilibrium against a suitable buffer.

Initially 24-hour samples, but later overnight samples, of urine were dialysed at 2 to 4° immediately after voiding against phosphate buffer *p*H 8·0 I = 0·02 in order especially to remove urea. Following repeated changes of buffer during 48 hours, the dialysed material, after centrifuging off any slight precipitate which formed, was freeze-dried in 10 ml. quantities in a centrifugal freeze-drying plant. The dry residue was reconstituted in 0·1 of the initial urine volume of distilled water to provide a solution of urinary proteins in phosphate buffer *p*H 8·0 I = 0·2. This solution was immediately dialysed for 24 hours at 2 to 4° against a large volume of phosphate buffer *p*H 8·0 I = 0·2 before electrophoretic and ultracentrifugal examination.

Serum samples were dialysed to equilibrium against phosphate buffer *p*H 8·0 I = 0·2 at 2 to 4°, and diluted with buffer to give a suitable protein concentration for subsequent examination.

Protein concentrations were determined refractometrically on the dialysed solutions of serum or urine proteins.

Electrophoresis Measurements.—These were made in phosphate buffer *p*H 8·0 I = 0·2 in the Tiselius (1937) apparatus at 0° and a potential gradient of 6. V/cm. Optical observations by the diagonal Schlieren method (Philpot, 1938) were photographically recorded on Ilford half-tone panchromatic plates, using a high pressure Hg arc as a light source from which monochromatic light λ = 546 mμ. was isolated by a suitable filter.

For the analysis of sera the total protein concentration was 2 g./100 ml. in each instance. For the urine protein analysis the total protein concentration was between 1·1 and 1·5 g./100 ml.

Ultracentrifuge Measurements.—The urine proteins were examined at concentration of 1 g./100 ml. in phosphate buffer *p*H 8·0 I = 0·2 + 0·15M NaCl. The solutions were subjected to 250,000 g. in the Svedberg oil-turbine ultracentrifuge using a 12-mm. cell, the optical recording being as described under electrophoresis.

Results and Discussion

In the Table the electrophoretic analyses of the sera from four cases of cadmium poisoning are presented together with the values for normal human serum obtained under the same experimental conditions. In two instances the proportion of gamma globulin is abnormally high and in all cases the alpha globulin proportion is slightly above the normal value. There seems, however, to be no uniformly consistent deviation from the normal attributable unequivocally to the effects of cadmium poisoning.

TABLE

THE ELECTROPHORETIC ANALYSIS OF SOME SERA FROM PATIENTS WITH CADMIUM POISONING

Serum Sample	Total Protein (g./100 ml.)	Electrophoretic Analysis			
			Globulins		
		Albumin	Alpha	Beta	Gamma
A3	7·25	53·8	9·2	16·6	20·5
B3	6·94	56·9	9·5	10·8	22·9
A1	6·84	65·7	9·9	12·0	12·4
B2	6·26	67·8	7·0	13·1	12·2
Normal values	6·75	65·1	6·4	15·1	13·6

In Fig. 1 electrophoresis and ultracentrifuge diagrams of the urinary proteins are given. Except in one instance the electrophoretic characteristics of the urinary proteins were similar to those shown in Fig. 1a, where there appears to be a very large number of ill-defined components covering a mobility range similar to that of the serum proteins. In the divergent case (A3, Fig. 1b) four relatively well defined components were present but in this patient the total urine proteins at about 0·5 g./100 ml. were very much higher than in any other instance.

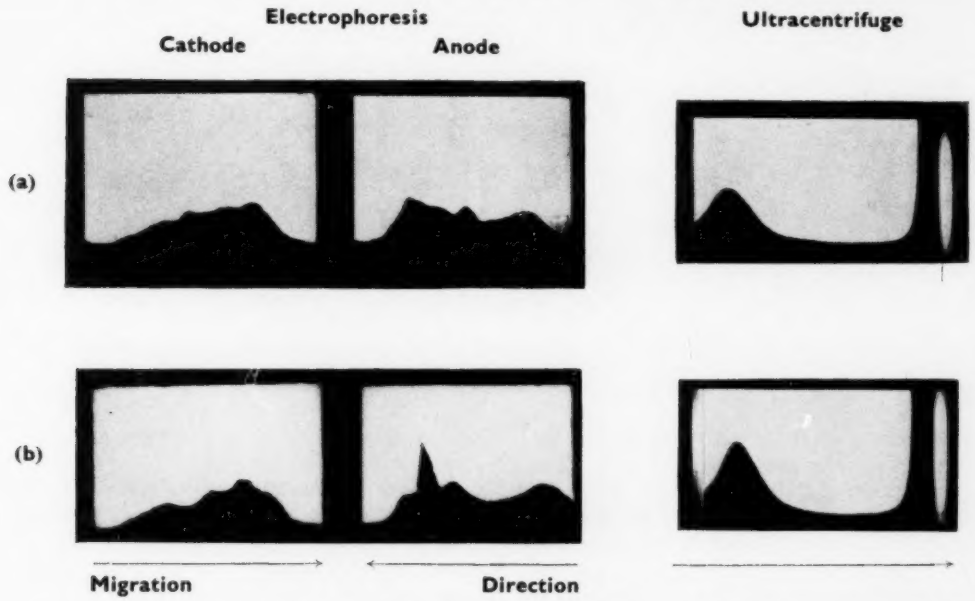

FIG. 1.—Electrophoresis and ultracentrifuge diagrams of urine proteins (*a*) Patient B3 : electrophoresis after three hours at 15 mA., *p*H 8·0 I = 0·2. (*b*) Patient A3 : ultracentrifuge after 80 minutes at 54,000 rev./min.

The urine proteins sedimented in the ultracentrifuge as a single component (Fig. 1), which is somewhat surprising in view of the complexity of the electrophoretic behaviour. Values for the sedimentation constant determined on solutions containing 1 g. protein/100 ml. varied from 2 to 2·2 S. These would correspond with a molecular weight in the range 20,000–30,000 which is very much lower than that of any known serum protein.

The data for the sera are similar in some instances to those given by Friberg (1950) : the sedimentation coefficients obtained for the urine proteins are of the same order as the values quoted by him. In general a more complex electrophoretic behaviour was observed for the urinary proteins, but this may have been due to the fact that Friberg in many cases concentrated the urinary proteins by precipitation with ammonium sulphate. This procedure may not have provided such representative preparations as would be obtained by freeze drying the total urinary protein.

Summary

The serum and urinary proteins from patients suffering from cadmium poisoning have been examined physico-chemically.

While the serum proteins show divergencies from the normal electrophoretic distribution, no characteristic deviation appears consistently.

The urinary proteins show a large number of electrophoretic components but sediment as a single component of a molecular weight in the range 20,000–30,000.

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AN ENVIRONMENTAL STUDY OF CASTING COPPER-CADMIUM ALLOYS

BY

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An environmental study to measure the concentrations of airborne cadmium oxide was carried out at the factories referred to by Bonnell on page 181, reporting the results of the clinical investigation of men exposed to cadmium oxide fume. Bonnell found that a number of these men had symptoms of chronic cadmium poisoning. Although the working conditions in the industry have improved in recent years, it was considered that knowledge of the present exposure to cadmium fume would be of interest both in assessing the present risk to health, and in providing information which might be of value should further cases occur.

In both factories the cadmium oxide was produced during the manufacture of copper cadmium alloys. Pure cadmium is first alloyed with pure copper to give a master alloy containing 33 or 50% cadmium at factory A, and 50% at factory B. The final alloy contains 0·5 to 1% cadmium, from which wire or sheet is made.

In factory A, both stages of the alloy manufacture were carried out in one workshop, shown diagrammatically in Fig. 1. In factory B the alloys were made in separate workshops (Figs. 2 and 3). Details of the processes involved in each factory are given by Bonnell on page 183.

Equipment Used in the Survey

A preliminary visit to the factories suggested that cadmium oxide was produced as a fume intermittently and was only part of the total airborne solid. At factory A the Rocker furnace was in continuous operation over a five-day week. At factory B the casting shop worked throughout a six-day week, while the special alloy shop was on day work only. The furnacemen, manhandling crucibles of molten

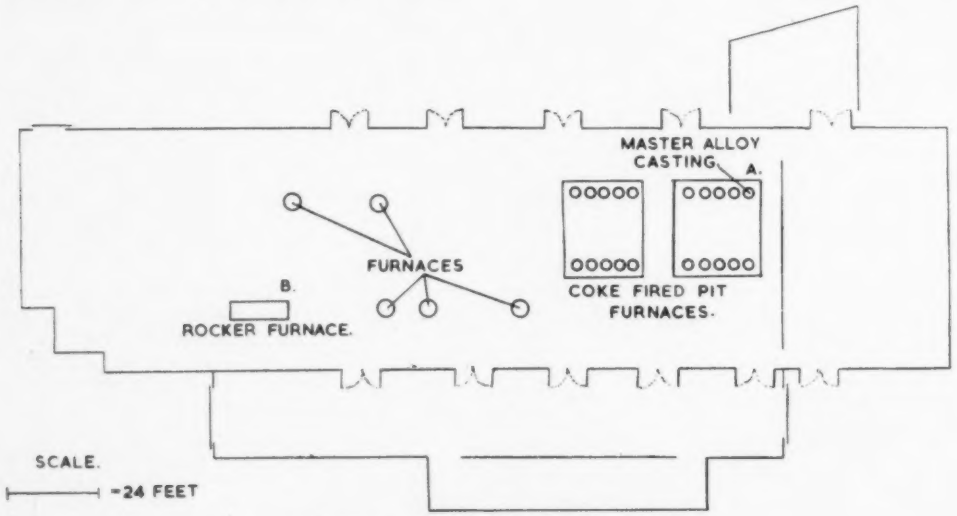

FIG. 1.—Diagram of cadmium alloy manufacture in factory A.

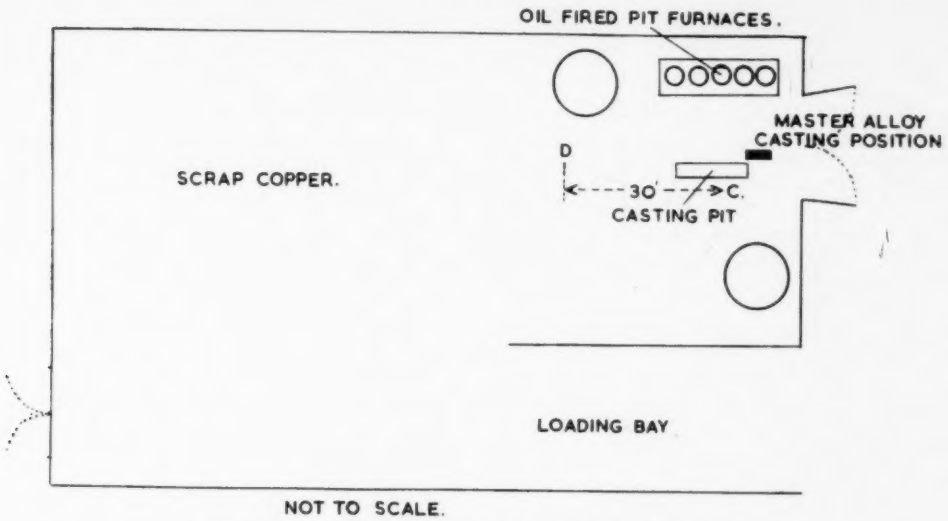

FIG. 2.—Diagram of master cadmium alloy manufacture in factory B.

metal, worked over an area of the workshops rather than in fixed positions.

The equipment used in the survey was chosen after consideration of the processes involved, and the conditions under which they were carried out. The requirement was for instruments to give mass concentrations, combined with particle size analysis, and to detect any unusually high concentrations which occurred during certain stages of the process.

Soluble Filter Pad.—The use of salicylic acid as a filtering material was reported by Briscoe, Matthews, Holt, and Sanderson in 1936. For this investigation, salicylic acid was unsuitable because it reacts chemically with cadmium oxide, and AnalaR dextrose was used in its place. The pads used were 1·5 cm. thick, in a 3 in. diameter filter holder, with an air flow of 5 to 6 cu. ft./min.

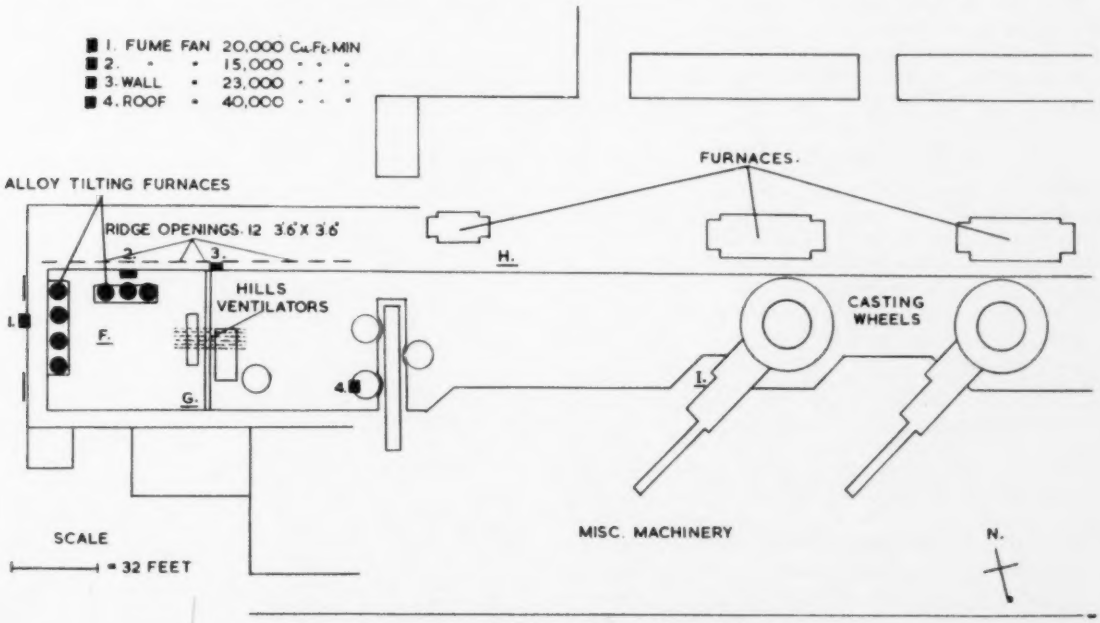

FIG. 3.—Diagram of final cadmium alloy manufacture in factory B.

measured by a gas meter. This equipment had been shown to give a high collecting efficiency, and could be left unattended for long periods under the conditions of low humidity found in the workshops.

In the laboratory the sample was dissolved in water and centrifuged to separate the solid fraction. A fraction of the supernatant dextrose solution was taken, and the cadmium content estimated. It was assumed that this represented the very fine particles which did not separate out either because of the viscosity of the solution or their partial solubility in neutral solution. The solid fraction was washed with water and alcohol, and a coarse separation into $> 5\ \mu$, from 5 to $0{\cdot}5\ \mu$, and $< 0{\cdot}5\ \mu$ fractions carried out by triple sedimentation in alcohol. The cadmium found in the supernatant liquid was added to the $< 0{\cdot}5\ \mu$ fraction. This procedure was used to give a semi-quantitative size distribution of the cadmium oxide.

The cadmium content of the samples was estimated on a polarograph at a half-wave potential of $-0{\cdot}7$ v, in 0·1 N ammonium chloride. The samples were found to contain copper in quantities sufficient to interfere with the cadmium wave, and a separation based on the solubility of cadmium sulphide in dilute hydrochloric acid (33% v/v) was carried out. The dry sample was dissolved in dilute hydrochloric acid (33% v/v) and the solution saturated with hydrogen sulphide. The copper sulphide was filtered off and washed with hydrochloric acid to dissolve any cadmium which had been precipitated with the copper.

The filtrate was heated to dryness and the residue dissolved in 0·1 N ammonium chloride for cadmium analysis on a polarograph.

Confirmation of the analytical technique was obtained from a series of recovery experiments. These were based on the estimation of a known added amount of cadmium under the varying conditions occurring during the analysis. A total of 38 experiments reproducing parts of the technique, with cadmium chloride as the cadmium source, gave an average recovery of 91%, with a standard deviation of 13.

A final series of experiments was performed on samples representing as closely as possible the unknown samples. A known weight of cadmium oxide (0 to 10 mg.) was mixed with copper oxide (0 to 2 g.) and dextrose (100 g.) for each of 13 samples. These were treated in the same way as the unknown samples, the only difference being that in the unknown samples the cadmium oxide was present as fume of very small particle size which did not separate from the dextrose solution, while in the prepared samples the cadmium oxide consisted of large particles and separated easily. Thus the bulk of the cadmium was found in different fractions in the two cases.

Of the 13 prepared samples, two gave anomalous results of 33 and 44% recovery. The remaining 11 gave a mean recovery of 81%, with a range of 72 to 94%. The anomalous results were probably caused by the nature of the cadmium oxide used. Polarographic analysis gave one low value of 66% in 10 weighed samples of cadmium oxide. The remaining nine gave an average purity of 98%, with a range of 83 to 108%.

The scatter observed throughout the recovery experiments was partly due to the polarograph used. To minimize this factor, the standard addition technique was adopted in all estimations, both in the recovery experiments and in the analysis of the samples.

Continuous Strip Recorder.—A continuous dust recorder based on the impingement of dust-laden air on to a celluloid strip is described by Hazard (1934), who used a photoelectric technique for estimating the dust on the resulting trace. The instrument used in this survey substitutes Whatman No. 1 strip filter paper for the celluloid moving across an orifice at 2 in. per hour, with air passing through the paper into the orifice at 4 l./min. The final record was used for visual observation, relating the intensity of the dust stain to times and processes, and for chemical analysis as required. The normal air pollution from furnace fuel and mould dressings gave a grey or black background marked with a brown coloration at each heavy emission of cadmium oxide.

Thermal Precipitator.—The thermal precipitator could not be used for quantitative measurements because of the high concentration of airborne dust other than cadmium oxide. In order to obtain a qualitative picture of the nature of the cadmium oxide emitted in the type of work involved, slides were taken near the Rocker furnace at factory A.

Investigation at Factory A

The workshop shown as Fig. 1 was engaged on general alloy production, including both master and final copper cadmium alloys. At one end of the workshop was a series of coke-fired pit furnaces, one of which (position A, Fig. 1) was used for the master copper cadmium alloy. At the centre of the workshop were a number of induction furnaces used for the production of alloys not containing cadmium. The Rocker furnace, used in the manufacture of the final cadmium copper alloy, was at position B, Fig. 1.

The numerous doors shown in Fig. 1, when opened, provided good general ventilation inside the workshop.

The separation of the processes in this workshop was such that in the first instance only the areas around the two furnaces using cadmium were considered to be of interest. A detailed description of the nature and operation of the furnaces used in the cadmium processes is given by Bonnell (1955).

Master Alloy

The alloy made during the survey was 33% cadmium in copper in a coke-fired pit furnace at position A in Fig. 1. The cadmium was first melted in the crucible, copper added, and the mixture stirred manually. When the alloy was ready for pouring a lid was placed over the crucible, which

was lifted from its pit, placed under an exhaust hood, and poured by mechanical means. The only fume emission observed occurred on removal of the crucible lid just before pouring.

The process was discontinuous, the master alloy being made in small batches as required by the Rocker furnace operation. Average values of 6, 5, 7, μg. cadmium per cubic metre air were found over three days. These low values were due to the discontinuity of the process, and the dexterity of the furnaceman in using the exhaust hood. Under the conditions observed it is unlikely that significant concentrations of cadmium oxide would occur in the general working atmosphere.

Final Alloy

The final alloy made during the survey was a low cadmium-content alloy prepared from pure copper and master alloy in a Rocker furnace, at position B Fig. 1. The pure copper was first heated to melting point, taking 40 to 50 minutes, and the required amount of master alloy was added. The furnace was then rocked for five to 10 minutes, and the resulting alloy poured into an oil-dressed mould. From the time the master alloy was added to the end of pouring an exhaust hood, placed in position by the furnaceman, covered the centre and mouth of the furnace. Cadmium oxide fume was emitted, violently at first, and to a lesser degree up to the end of pouring. There was an obvious loss of fume from around the exhaust hood during pouring, and also some leakage from one end of the furnace.

The sampling equipment was placed 8 ft. from the furnace in such a position that the furnaceman was normally in the area between the equipment and the furnace, except during the rocking procedure, which he controlled from the far end of the furnace. The concentrations found thus represent a minimum rather than maximum exposure to cadmium oxide fume of persons working near the furnace.

The strip recorder gave a grey background trace, with black patches corresponding to the times when the Rocker or adjacent furnaces were pouring. In addition, peak emissions of cadmium oxide caused brown patches to show through the background.

The thermal precipitator was used at an earlier visit to the factory to take samples near the Rocker furnace at times of peak emission of fume. Photographs of three slides are shown (Figs. 4, 5, and 6).

The dextrose pad equipment was operating continuously over a five-day working week. The sample pad was changed at the end of each shift. Each furnaceman normally cast eight billets, of 5¼ cwt. each, per shift. On one shift, day 5, shift 1 (Table 1), only one billet was cast because of the absence of the regular furnaceman.

The mass concentrations of cadmium, with the average size distribution, are given in Table 1.

TABLE 1
CADMIUM CONCENTRATIONS AT THE ROCKER FURNACE AT FACTORY A

		Concentrations (μg. Cd/m.³ Air)				
Shift	Time	Day 1	Day 2	Day 3	Day 4	Day 5
1	06.00–14.00	72	59	21	89	13
2	14.00–22.00	48	19	16	31	23
3	22.00–06.00	31	34	37	35	38

Average size distribution $> 5\mu = 4\%$ by weight, $0{\cdot}5\mu$ to $5\ \mu = 5\%$ by weight, $< 0{\cdot}5\ \mu = 91\%$ by weight.

Results

Throughout this paper the cadmium concentrations in the atmosphere have been given as average values, although in most cases the strip recorder showed that the nature of the work caused a comparatively high concentration for some 15 minutes of each hourly casting cycle. At other times there was insufficient cadmium present in the atmosphere to be seen through the black background caused by the burning oil. The mixing and casting operations gave rise to a dense yellow cloud of cadmium oxide fume at the mouth of the furnace or crucible which diffused and circulated according to local air movement. The exposure of the furnacemen at these times was entirely dependent on the care taken to avoid direct contact with the fume cloud, a very variable factor. Ideally, sampling equipment should have been used to monitor each furnaceman, but apart from the psychological effect on the men concerned, the conditions of working made this impossible.

Chemical analyses were performed on some of those sections of the strip records corresponding to the periods of peak emission, usually of about 15 minutes' duration. At factory A, position B, taking in both cases the average for four shifts, the concentrations at the peak times varied from 1·5 to 3 times the over-all concentrations. At factory B, position C, for one day, the average peak emission concentration was 450 μg. Cd/m.³, compared with an average of 132 μg. Cd/m.³ for the whole time. These concentrations were measured at positions some distance from the source of the cadmium oxide fume, and some diffusion of the fume cloud must have occurred before it was recorded.

Investigation at Factory B

Master Alloy.—The master alloy, containing 50% cadmium, was made in the special alloys workshop, shown as Fig. 2. This workshop was used as a

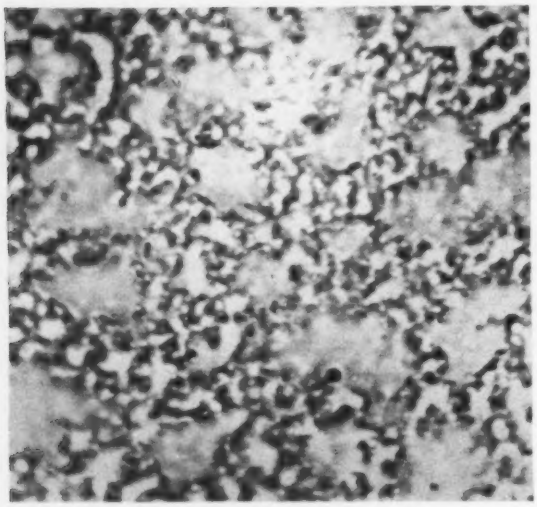

FIG. 4.

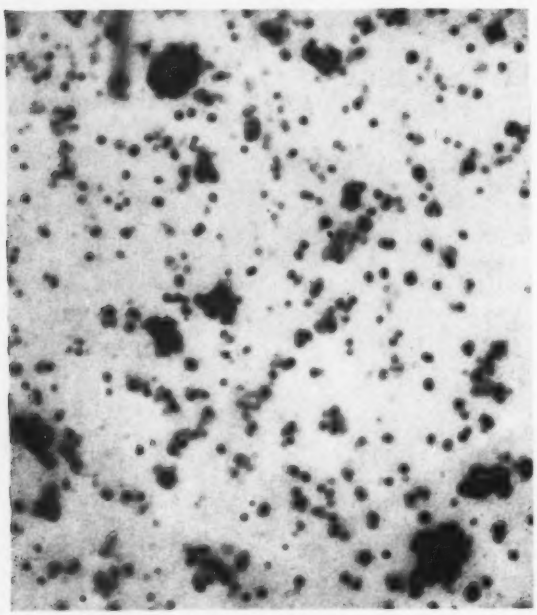

FIG. 5.

FIG. 4 (× 2,000).—Taken near the mouth of the furnace. This shows the fume nature of the cadmium oxide immediately on contact with the outside air.

FIG. 5 (× 2,000).—This was taken 3 ft. from the mouth of the furnace. This is probably the form in which the cadmium oxide usually occurs in the general atmosphere.

FIG. 6 (× 2,000).—This shows the cadmium oxide which was leaking from one end of the furnace. In this case the cadmium had travelled from the centre of the furnace, probably as metal fume, and had been oxidized at a lower temperature to give larger particles.

general store for scrap copper, with associated handling equipment, except that it also contained a series of oil-fired pit furnaces and a brass recovery furnace. One of the pit furnaces was used for the master alloy, while the remainder made other alloys, including one of a lower cadmium content. The furnacemen were normally the only occupants of the workshop, and rarely moved away from the vicinity of the furnaces. They were on day work only.

The copper was first heated, and, when it was molten, the cadmium was added, a few sticks at a time. The mixture was stirred manually during this time. The crucible was finally lifted from its pit by an overhead crane and moved to the casting position, where it was tilted by hand and poured into a number of small moulds. Throughout the last stages of the process there was a continuous emission of cadmium oxide fume, the bulk of which was carried by convection to a small exhaust fan near the roof and discharged into the outer atmosphere. During the investigation the master alloy was made only on days 7, 8, and 9 (Table 2).

Sampling equipment was set up at position C, Fig. 2, to measure the cadmium content of the atmosphere in the main working area, and at position D to obtain values at the perimeter of this area.

Oil dressings for the moulds used by the furnaces not making the master alloy caused a heavy background trace on the strip recorder. This background disappeared very quickly at the end of the working day, suggesting good ventilation of the workshop. At position C, brown patches showed through the

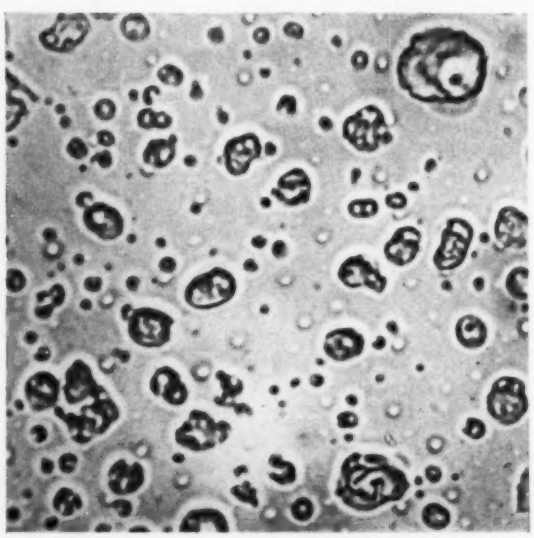

FIG. 6.

TABLE 2

CADMIUM CONCENTRATIONS AT MASTER ALLOY WORKSHOP AT FACTORY B

Position	Cadmium Concentrations (μg. Cd/m.³ Air)									% by Weight Average Size		
	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	> 5 μ	0·5 – 5 μ	<0·5 μ
C	12	45	46	—	28	34	132	118	93	13	10	77
D	4	34	11	—	11	10	55	69	77	5	6	89

The master alloy was made on days 7, 8, 9 only.

background corresponding to the times at which the alloy was made and cast. These patches did not occur on the strip recorder at position D, indicating that peak concentrations did not reach this point.

The results are summarized in Table 2.

The mass concentration figures showed the expected differences between positions C and D except on the final day. Because of the construction of the workshop, outside weather conditions could have resulted in a more general distribution of fume on that occasion.

Final Alloy.—Fig. 3 shows the lay-out of the workshop concerned in the manufacture of the final alloy at factory B. This workshop was largely concerned with processes in which no cadmium was used, from the refining of copper to the machining of the finished bars and billets. At one end of the workshop was a series of oil-fired tilting furnaces used for the final cadmium and other copper alloys. Each of the furnaces was covered by an exhaust hood which had to be partly displaced by the furnaceman during loading and mixing operations. In addition to the separate exhausts of these furnaces, this end of the workshop had general ventilation provided by the fans and openings shown in Fig. 3.

The copper was first heated to melting point in the crucible of the furnace, and the master alloy was then "tossed" in by the furnaceman. The mixture was stirred by hand with a pole, and the crucible tilted mechanically to cast the alloy into a mould below. During the latter processes, cadmium oxide fume could be seen escaping from under the exhaust hood and rising to roof level.

Sampling position F (Fig. 3) was 6 yards in front of the furnaces, and was the centre of the area used by the furnacemen except when operating the furnaces. The concentrations at this point therefore give average exposures, and do not include possible high intermittent exposures when mixing the alloy in the crucible. Sampling position G was the extreme limit of movement of the furnacemen during normal operations. Equipment was installed at positions H and I to measure the concentrations in parts of the workshop remote from the source of cadmium oxide.

Contamination from the oil fuel and mould dressings caused a dense background on the strip recorder at all positions. Only at F was any suggestion of the brown coloration caused by cadmium fume observed against this background.

The dextrose pad equipments were operated continuously over the sampling period, the pads being changed morning and evening. The concentrations found are given in Table 3.

The average concentrations at position F showed two trends. In general the levels at night were higher than those of the corresponding day. This was probably due to the closing of doors and

TABLE 3

CADMIUM CONCENTRATIONS AT FINAL ALLOY PRODUCTION AT FACTORY B

	Cadmium Concentrations (μg Cd/m.³ Air)																Mean Size Distribution (% by weight)		
	Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8				
Position	a.m.	p.m.	a.m.	p.m.	a.m.	p.m.	a.m.	p.m.	a.m.	p.m.	a.m.	p.m.	a.m.	p.m.	a.m.	p.m.	>5 μ	0·5–5 μ	<0·5 μ
I	1	—	15	5	4	3	40	—	—	2	2	3	1	4	2	5	3	11	86
H	—	—	1	4	9	3	16	—	—	3	5	5	7	5	4	5	8	22	70
G	10	11	5	16	45	51	86	—	—	84	57	35	13	39	42	39	4	8	88
F	—	48	29	—	127	127	270	—	—	154	212	79	80	43	60	48	6	9	85
	Mean wind speeds in knots at meteorological station 10 miles S.W. of factory																		
Speed	5		8·7		14·2		15·2		14·9		11·6		6·2		10·9				
Direction	120°		150°		130°		140°		130°		80°–30°		150°		90°				

Sample at position H contaminated by sparks from nearby reverberatory furnace.
The workshop was closed for one 24-hour period between days 4 and 5.
a.m. = 10 p.m.–10 a.m. (Day 4 to 6.30 a.m.).
p.m. = 10 a.m.–10 p.m. (Day 5 from 7.30 a.m.)

consequent lack of natural ventilation at night. The second trend was a rise in concentrations on the middle days of the sampling period, and a subsequent fall later in the week which could not be correlated with the rate of working. The variations in wind speed obtained from a meteorological station 10 miles S.W. of the factory over this period suggest that weather conditions might affect ventilation of the workshop.

The mass concentrations at positions H and I suggest that there was no appreciable airborne cadmium oxide in those parts of the workshop distant from the cadmium operations.

Discussion

Friberg (1950) found a high incidence of chronic cadmium poisoning amongst workmen in factories manufacturing alkaline accumulators. The atmospheric concentrations of cadmium were found to be 3 to 15 mg./m.^{3}. Princi (1947) reported concentrations of 0·04 to 1·44 mg. Cd/m.^{3}, with no cases of poisoning. Hardy and Skinner (1947) as a result of investigating a smaller group of men making cadmium-faced bearings, suggested that chronic cadmium poisoning might occur. They reported an average atmospheric concentration of 0·1 mg. Cd./m.^{3}. Friberg (1950) concludes from the evidence of these papers and his own findings that the maximum allowable atmospheric concentration of cadmium of 0·1 mg./m.^{3}, given by the American Conference of Governmental Industrial Hygienists (1954) should provide a satisfactory margin of safety.

The atmospheric concentrations found in factories A and B during this investigation cannot be strictly compared with those quoted above, because of differences in the nature of the cadmium and in general working conditions over the past years. The concentrations given in this paper relate to cadmium, as cadmium oxide, in the form of fume, which would be absorbed more rapidly and completely than the dust reported by Friberg (1950).

The present working conditions at factories A and B differ greatly from those of 1939–45, when "blackout" greatly reduced normal ventilation at night, and the chronic nature of the poisoning suggests that past conditions may be responsible for the present symptoms. In addition, since 1948 various improvements have been made in the ventilation of the processes used in these factories.

In factory A the exhaust system over the furnace for the manufacture of the master alloy was introduced, and although no data are available for atmospheric concentrations before its introduction it can be assumed that the cadmium levels near the furnace were very much higher at that time. The Rocker furnace has been in operation for about 19 years, originally without an exhaust hood. The concentrations at this point (position B, Fig. 1) arose from the manufacture of a low cadmium-content alloy. There appears to be a personal factor amongst the furnacemen, shift 1 giving higher levels than shift 2. The more constant and lower levels of shift 3 at night, when the workshop doors were closed, suggest that in the absence of cross air currents, the exhaust system was sufficient to prevent a rising concentration of cadmium fume inside the workshop.

At factory B, the manufacture of the master alloy gave lower concentrations than would have been expected for a furnace not equipped with an exhaust hood. It could be seen that the convection effects of this type of furnace carried the cadmium oxide fume as a well-defined pillar to the exhaust fan near the roof. The natural ventilation from the nearby door dispersed residual fume, as shown on day 9, Table 2, when the air movement was towards the remote end of the workshop. Under the conditions observed changes of wind could have caused wide variations in the cadmium oxide levels in the vicinity of the furnaces. This process had previously been carried out in a different workshop, and although no quantitative assessment was possible it was unlikely that a similar fortunate arrangement of ventilation applied.

The concentrations found during the manufacture of the master and final alloys at factory B were not proportional to the amount of cadmium used in the processes, and suggest that the percentage loss of cadmium to the air was greater in the manufacture of the final alloy. The three days, 7, 8, and 9 (Table 2), when the master alloy was produced supplied sufficient master alloy for several days' production of final alloy, and yet gave comparatively low concentrations in the atmosphere. This is also evident from Table 2, where the manufacture of a 7% alloy from master alloy and copper on days 2, 3, 5, and 6 gave concentrations of about 30% of those due to the master (50%) alloy. The probable explanation is the temperatures involved in the processes.

The variations in the concentrations found during this survey, together with the changes in working conditions that have taken place in recent years, make it impossible to relate concentrations of airborne cadmium to the incidence of cases of poisoning. Thus on the present evidence no definite conclusions regarding safe working conditions can be reached, but future routine atmospheric and medical examinations may provide sufficient information upon which to base recommendations.

Summary

Mass concentration levels of cadmium as cadmium oxide fume in the atmosphere of the two factories making copper cadmium alloy are reported. Air samples were taken during five days at factory A and nine days at factory B.

The values at four of the positions represent the minimum concentrations to which the furnacemen operating the cadmium processes were exposed. Other values were obtained giving the exposure of vicinity workers.

The significance of these results is discussed.

I should like to thank the management of the two factories concerned, particularly the medical and personnel departments, also Dr. Donald Hunter and Dr. D. G. Harvey for their encouragement and ready assistance. The polarographic estimations were carried out by Miss Jean Peal, and Messrs. Casbolt and Biles gave valuable technical assistance.

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The values at four of the positions represent the minimum concentrations to which the furnacemen operating the cadmium processes were exposed. Other values were obtained giving the exposure of vicinity workers.

The significance of these results is discussed.

I should like to thank the management of the two factories concerned, particularly the medical and personnel departments, also Dr. Donald Hunter and Dr. D. G. Harvey for their encouragement and ready assistance. The polarographic estimations were carried out by Miss Jean Peal, and Messrs. Casbolt and Biles gave valuable technical assistance.

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DISABLING PNEUMOCONIOSIS FROM LIMESTONE DUST

BY

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Limestone dust is generally regarded as being relatively harmless. In this paper I wish to record eight cases of pneumoconiosis in limestone workers, in all of which limestone played the sole or principal aetiological part.

My attention was first drawn to the condition in November, 1950, when I saw the chest radiograph of a patient whose occupation was limestone crushing. The appearances were most suggestive of pneumoconiosis.

Pneumoconiosis in a Limestone Grinder

Case 1.—The patient, A. W., was 52 years of age in 1950. After spending two years as a blacksmith's apprentice and six months as a labourer in a whinstone quarry, he served through World War I. He then worked for one year as a diver's assistant and six months as a shipyard labourer before becoming a limestone grinder in 1921. He continued at this work until 1947 when he left to receive medical attention for a swelling in the left upper part of the neck, which had been gradually increasing in size for a year, and for blockage of the left nostril of three months' duration. A tumour was found in the posterior nares which on biopsy was reported to be a fibrosarcoma. *X*-ray examination of the lungs showed bilateral mottling which might have been due to pulmonary metastases or pneumoconiosis. From January until July, 1947, he was given *x*-ray therapy to the nasopharynx and to both sides of the neck, but not to the chest. In November, 1947, his condition was satisfactory and there was no evidence of a primary lesion or of secondary glands. The *x*-ray appearances, however, had not changed much since then, although about March, 1950 (Fig. 1), he complained of increasing breathlessness and gave up the light job of storekeeper he had held for the previous two years. Examination in December, 1952, showed that dyspnoea was absent at rest, but present on slight exercise. Cough and sputum were troublesome in the morning, but not during the day. He was in poor general condition, being thin and pale. There was no finger clubbing. The chest was flattened, expansion 1¼ in., percussion note hyper-resonant, breath sounds vesicular, and post-tussic crepitations, audible at both bases, were particularly numerous on the right side.

FIG. 1.—Case 1 in March, 1950, aged 52 years limestone grinder for 26 years.

The heart was normal but the peripheral vessels showed evidence of arteriosclerosis. There were no enlarged cervical glands and the throat and nose seemed normal. An *x*-ray examination in March, 1950, showed a normal appearance of the thoracic skeleton, heart, and diaphragm. Nodular opacities were present in both lungs, fairly uniform in size (3 to 4 mm. in diameter), profuse and evenly distributed throughout the right lung but present on the left side mainly in the mid-zone. At the right infraclavicular area there were some patches of coalescence, one of which measured 1 cm. in diameter. At the left base the translucency was much increased denoting emphysema (or possibly a localized pneumothorax). The appearance was that of early complicated

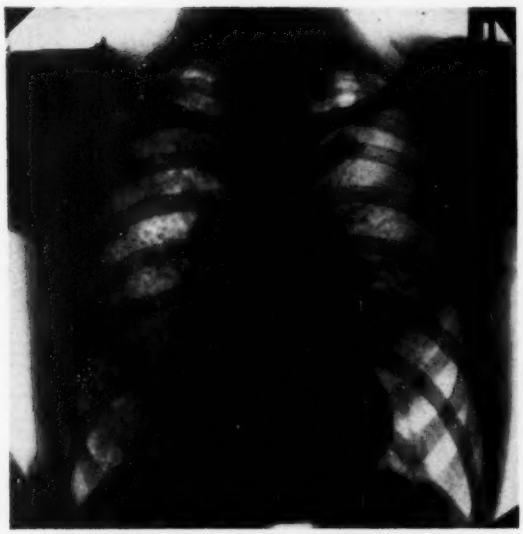

FIG. 2.—Case 1 in May, 1954.

pneumoconiosis, category (3)A.* In May, 1954, the nodulation had become denser, and, in places, a little larger, with slightly increased coalescence but without the formation of definite masses. The hilar glands now showed egg-shell calcification and some of the parenchymal nodular elements were proably also partially calcified (Fig. 2).

The patient has been granted a certificate of total disability on account of silicosis from the Pneumoconiosis Medical Panel.

Geology of Limestones

Limestones consist predominantly of calcium carbonate and occur widely in rocks of all ages with the exception of Pre-Cambrian rocks in which they are seldom found. They are formed in three principal ways. Organic limestones are built up from the skeletal remains of a great variety of organisms, plant as well as animal, deposits in the form of calcite being by far the most abundant. Chemical limestones are formed by the precipitation of calcium carbonate. Clastic limestones are formed by erosion and redeposition of preformed limestones. They are of less importance. Special varieties of limestones include magnesium limestone, which contains a notable proportion of magnesium carbonate, and dolomite rock, a limestone in which the mineral dolomite forms the bulk of the rock, dolomite being the double salt, calcium-magnesium carbonate.

* The classification adopted is the International Scheme for the Classification of Radiographs in Some of the Pneumoconioses, recommended in the Report of the Third International Conference of Experts on Pneumoconiosis (Sydney, 1950).

Limestones play an important part in a wide variety of industries. They are extensively employed in agriculture for improving the soil, either as the pulverized natural rock (ground limestone), or, after burning, as lime, also for poultry grit, and in the feeding of pigs and other farm stock. In the building and allied trades limestones form an important supply of building stone, as, for example, Portland stone, which is the principal building stone used in London. They are also used for monumental work, for making artificial stone, as aggregates for concrete, as roadstone, and for making Portland and other kinds of cement. Some limestones take a high polish and are commercially known as marbles. In the strict petrological sense, however, marbles are crystalline rocks composed of interlocking grains of calcite. They result from the crystallization of pure limestones under the influence of increased temperature and pressure, and hence are metamorphic rocks. In the chemical industry limestone is used as a base, as a source of lime, for the manufacture of carbon dioxide, and for making calcium compounds. It is an important raw material in the metal industry, being used as a flux in various smelting and melting operations, for instance, in the working of blast furnaces. In the coal-mines powdered limestone is extensively used for stone dusting to reduce the risk of explosions. To a less extent, it is employed in the manufacture of paints and distemper, of paper, glass, soap, pottery, medicinal and pharmaceutical preparations, explosives, in the textile and printing trades, in railway engineering, in furnace construction, and as a mild abrasive in metal polishing.

Brief Review of the Literature

According to Forbes, Davenport, and Morgis (1950) many authorities considered that the dusts encountered in the marble, gypsum, cement, lime, and limestone trades were the least harmful of inorganic dusts. Some even spoke of their having a beneficial action on tuberculosis. Earlier in the century, however, several Italian observers reported an increased incidence of pulmonary disease in such workers, particularly in cement works. The relationship of cement to chronic pulmonary disease is somewhat obscure. As far as Portland cement is concerned, however, it seems unlikely that cases of pneumoconiosis accompanied by disability occur. This material can hardly be regarded as entirely inert, since it is irritating to the skin and, mildly, to the upper respiratory passages, but it does not appear to produce pulmonary fibrosis of a significant degree. The evidence for this includes the studies of Gardner, Durkan, Brumfiel,

and Sampson (1939) who examined and radiographed 2,278 workers in cement, of whom over 55% had been exposed for more than 10 years. No cases of disability were met with and *x*-ray abnormalities were minimal, leading the authors to conclude that the dust risk in this industry was trivial. Dervillée and Carrère (1935), who studied 250 men engaged in making cement and 300 using it, found no evidence of any pulmonary damage from the dust. Parmegianni (1951) carried out *x*-ray examinations of 5,213 workers in the cement industry, of whom 2,473 were miners and quarriers in the marl beds, 1,348 in the asbestos-cement industry, 533 in the manufacture of cement, and 859 were in miscellaneous or unclassified occupations. Cases of silicosis, diagnosed on radiological grounds only, were found, but the incidence was much less than in the other dusty Italian industries and almost confined to those who were in contact not with cement but with the raw materials from which cement is made. The greatest frequency and seriousness of the disease was in the rock-miners and quarriers, in whom there were 181 cases of reticulation (7·4%), 21 cases of nodular silicosis (0·8%), and six cases of massive silicosis (0·2%). In the cement manufacturing processes, while there were 27 cases of reticulation (5·1%), no cases of nodular or massive silicosis were discovered.

Bianchi and Turano, according to Forbes and his colleagues (1950), independently studied Italian marble workers and found cases of chronic bronchitis and pulmonary emphysema without much functional impairment or typical *x*-ray changes. Gardner and Dworski (1922) exposed guinea-pigs to marble dust and found that this was soluble in the lung tissue, that it aided calcification in pre-existing tuberculous lesions, but that insoluble matter caused a small degree of fibrosis after prolonged exposure, and delayed the resolution of the inflammatory process. Dreessen (1934), out of 422 marble finishers, examined 80, chosen principally to include men with longer exposures. Sixty had more than 10 years' experience, 48 more than 20 years', 30 more than 30 years', and 11 more than 40 years'. He found that, in a certain number of cases, the dust had produced a mild bilateral linear fibrosis, but no serious lung changes were noted, and there was no disability even after long exposure. He regarded his findings as essentially negative. Fazzi (1951), however, reports as a case of silicosis a man aged 54 years who had worked for 38 years cutting and drilling with pneumatic tools white marble, the silica content of which was stated not to rise over 0·27%. The *x*-ray findings showed bilateral nodulation, said to be typical of silicosis, but the possibility of concomitant tuberculosis was not entirely eliminated.

Gypsum and alabaster are hydrated calcium sulphates. Manfredi (1949) noted cases of chronic bronchitis and emphysema in a clinical and radiological study of 30 alabaster workers. Gardner (1938) found no evidence of silicosis in men exposed for many years to gypsum dust, and was impressed by the protective action of this dust when mixed with high concentrations of quartz when it was administered to animals. A suggestion that lime exerts a beneficial modifying influence on silicosis is contained in an annotation in the *British Medical Journal* (1952) as explaining the lesser incidence of silicosis in the Kolar goldfield in South India compared with that in the Witwatersrand. At Kolar the amount of lime in the airborne dust is between 10 and 12%, in the Witwatersrand 0·6 and 4·2%. Koelsch and Kaestle (1929), after examining 82 persons who had worked in shell limestone only, concluded that, under certain conditions and over a long period, limestone could cause pulmonary changes within the meaning of " dust lung ".

The latest report is that of Raymond, Sivadon, and Conil (1952) who examined 41 limestone quarrymen and stone cutters and found 19 showing some radiological changes, consisting essentially of enlarged hilar regions, increased vascular markings, calcified lymph nodes and aortic enlargement, but without any nodulation or massive shadow formation. Several of the men had symptoms and signs of bronchitis with a tendency to emphysema. The stone consisted almost entirely of calcium carbonate with a total silica content of 1·5 to 4·3%, the free silica being 0·7 to 2·9%. The authors believe that the condition is not accompanied by progressive fibrosis and that limestone dust is allied to Gardner's inert dust.

Limestone Grinding

The limestone is received at the grinding factory as ½-in. chips and after passing through screens is dried in rotary driers, ground in three successive mills, and finally bagged. The screens produce much dust but this part of the factory is separate from the remainder and no one enters it except for oiling and maintenance when the machinery is at rest. Exhaust ventilation is applied to the rotary driers and to the mills. When I first visited the factory in 1950, the dust removed at these points was simply discharged into the open air above roof level. As the factory is situated in the country this procedure did not cause any nuisance. No exhaust was applied at the bagging points, and considerable quantities of dust were given off at this and other

places, producing a visible haze in the atmosphere of the workroom and thickly covering the clothing and faces of the workers.

Different grades of fineness of ground limestone are produced. For agricultural purposes it is unnecessary and even inadvisable for the limestone to be ground to a very fine degree, but for stone-dusting in mines a relatively fine product is required. Regulations under the Coal Mines Act, 1945, require the limestone to be ground so that all of it passes through a 60-mesh sieve and not less than 50% nor more than 75% passes through a 240-mesh sieve. Even in producing the coarser grades, however, much very fine dust is evolved. It is unfortunate that it has not been found possible to have studies made of the size, concentration, and constitution of the airborne dust particles.

All 15 employees at this factory normally work in one workroom. As they are employed according to the needs of the moment, all have had experience of all the processes, including the supervision, maintenance, and repair of plant, bagging, loading, and other incidental jobs. While the dust exposure of individual workmen varies somewhat, those having carried out bagging operations to a greater extent than their fellow workers no doubt having had greater exposure, it is impossible to differentiate between the work done by the various men. Their exposure to limestone dust must therefore be taken as differing mainly in regard to their duration of employment. In this account the terms " grinder " and " grinding " relate to men employed and processes carried out in this factory, including the processes incidental to grinding. Of the 15 men, eight had more than five years' exposure to limestone dust, and clinical and radiological examinations were made of these.

Four Other Cases in Grinders

Case 2.—M. S., aged 50 years, was exposed to limestone dust for 20 years, three years quarrying and 17 years grinding. He had had no previous occupation other than that of butcher. He complained of cough, sputum, and tightness of the chest for four or five years with increasing dyspnoea for three years. He had bronchitis in March, 1951.

Examination showed a man of average nutrition, good colour, no cyanosis, no finger clubbing. Chest expansion was 2½ in., equal on both sides, the percussion note was normal, breath sounds were vesicular though harsh at the left apex, and a few crepitations were heard at the right base posteriorly and dispelled by cough. Several sputum tests and a laryngeal swab were negative for *M. tuberculosis*.

An *x*-ray examination in October, 1951, showed a normal skeleton, heart, and diaphragm. At the right apex, the right and left infraclavicular areas, and the right and left mid-zones were areas of diminished translucency, irregular in density and shape, and shading imperceptibly into more translucent lung tissue without any recognizable margins. The areas between the infraclavicular and mid-zones showed a ground-glass appearance with some very fine stippling. Subsequent films showed little change until May, 1954, when it was seen that the disease had progressed, the areas of diminished translucency were denser with better defined margins, the stippling had become coarser, and the picture (Fig. 3) was now typical of pneumoconiosis with advanced massive shadows of category (3)C.

Case 3.—A. M., aged 58 years, a limestone grinder for 28 years, was previously a road repairer for two years, and a kiln drawer at a fireclay brickworks for 14 years. He enjoyed good health except for slight cough attributed to smoking 20 cigarettes daily. He had no sputum or dyspnoea except after heavy smoking. He had no previous respiratory or other serious illness. He was of slight build, of a good colour, with no clubbing. Chest expansion was 1¾ in., the contour was good, movements were equal on both sides, but the percussion note was impaired at the right base posteriorly where also vocal resonance was slightly diminished. Breath sounds were normal, with no accompaniments. Heart sounds were normal. Exercise tolerance was good.

Radiographs showed the heart as normal in size but slightly displaced to the right. The right interlobar septum was thickened, distorted, and displaced slightly downwards. Fluffy irregular shadows were present at both bases, particularly on the right, with smaller, fainter shadows in the mid-zones extending into the upper thirds of the lung fields. Calcified spicules were seen in the left mid-zone as well as in the hilar glands. There were emphysematous bullae at the right base. The general appearance (Fig. 4) was suggestive of complicated pneumoconiosis, category (3)A.

Case 4.—W. H., aged 41 years, had been grinding limestone for 18 years, and before that was a farm worker. He had always enjoyed good health, and regarded himself as very fit at the time of examination. He had occasional cough at night but no sputum or dyspnoea. He looked well, though thin, had a good colour and no clubbing. Chest expansion was 2½ in., and there were no abnormal signs in the heart or lungs. There was no cervical adenitis, and the throat and mouth were normal except for early pyorrhoea. Exercise tolerance was normal.

Radiographs showed an increased slant of the lower ribs, widening of the intercostal spaces, and the diaphragm depressed to the level of the twelfth rib. The heart shadow was normal. There was generalized reticulo-nodulation in both lung fields, individual elements being small (2 to 4 mm.), slightly blurred, and not very dense. The appearance was typical of early simple pneumoconiosis (Fig. 5), category 2 (upper limit).

Case 5.—R. C., aged 48 years, had been grinding limestone for 16 years. Before that he had been employed for five years in a whinstone quarry and for six months in an ironstone pit. His other occupations

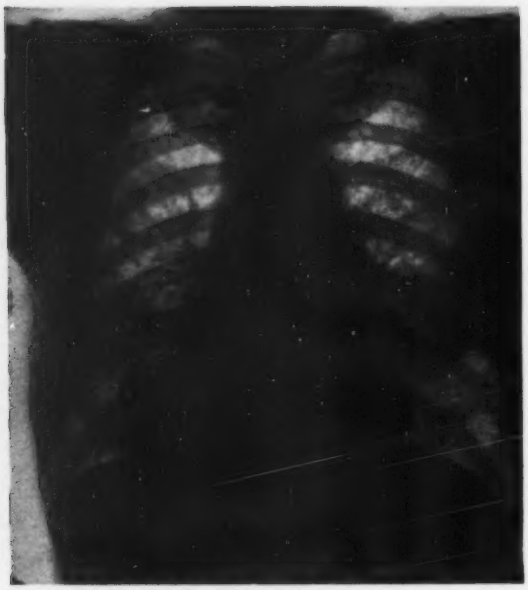

FIG. 3.—Case 2 in May, 1954, aged 53 years; limestone grinder for 20 years.

FIG. 4.—Case 3 in September, 1951, aged 58 years; limestone grinder for 28 years.

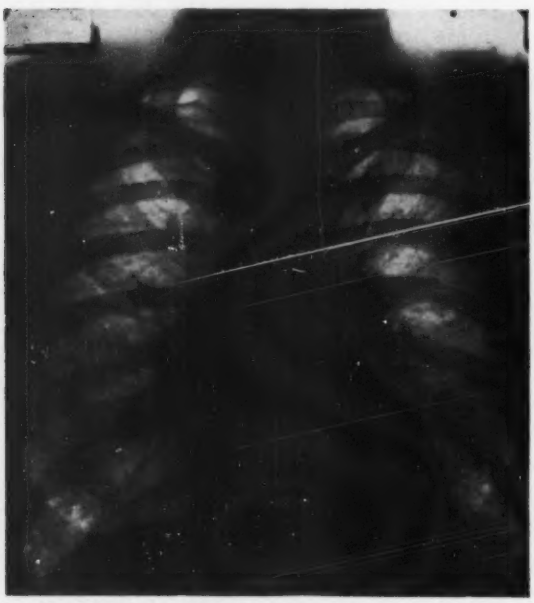

FIG. 5.—Case 4 in September, 1951, aged 41 years; limestone grinder for 18 years.

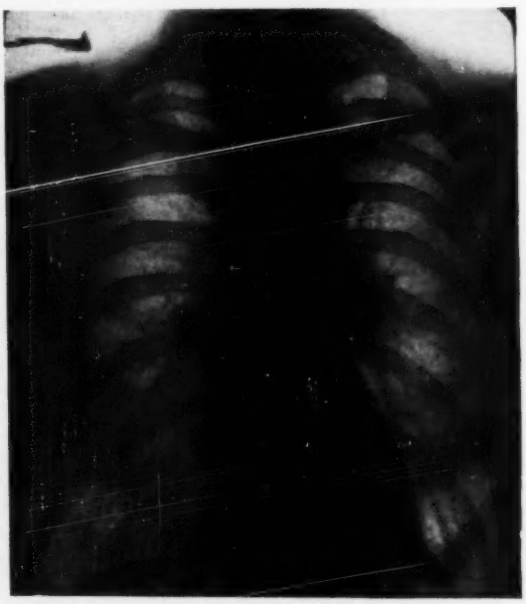

FIG. 6.—Case 5 in September, 1951, aged 48 years; limestone grinder for 16 years.

were not dusty. His previous health had been good, he felt fit and had no symptoms whatever. He looked healthy, and musculature, colour, and nutrition were good. No finger clubbing was seen. He had a congenital (probably familial) deformity of the sternum. Chest expansion was 2 in., and percussion and auscultation of the lungs normal. Heart sounds were normal, and no abnormalities of nose, throat, or neck glands were found. Exercise tolerance was good.

Radiographs showed normal skeleton and heart shadows. The left dome of the diaphragm was blurred and the left costophrenic angle obscured. Reticulo-

nodulation in both mid-zones, nodulation most marked on the left, was seen, and some increase in the hilar shadows. The appearance (Fig. 6) was that of simple pneumoconiosis, category 3.

Grinders without Pneumoconiosis

The remaining four limestone grinders were found not to have pneumoconiosis.

W. L., aged 44 years, had been a limestone grinder for seven years. He was unable to give an accurate account of previous occupations which had included farm work, labouring in a steel-rolling mill, and work in a whinstone quarry. He had had two attacks of pleurisy in adult life, otherwise his health was always good. He had morning cough, but no sputum, or dyspnoea. He was thin, of a good colour, with no finger clubbing. Chest expansion was 2¾ in., and no abnormalities were detected on examination of the heart, lungs, cervical glands, or throat.

Radiographs showed slightly accentuated lung markings and increased translucency of both bases but no parenchymal opacities.

D. B., aged 39 years, had been a limestone grinder for 20 years with no previous exposure to dust. He enjoyed excellent health, had no symptoms, looked very fit, had a chest expansion of 3¼ in., and on examination appeared quite normal.

Radiographs were normal apart from some increase in vascular markings at both bases.

F. G., aged 43 years, had spent his entire working life either limestone grinding (approximately 15 years) or whinstone quarrying (about 14 years). He had always had good health. He had morning cough and sputum but no dyspnoea. No abnormalities were found on clinical examination ; chest expansion was 2½ in.

The *x*-ray appearances were normal except that the dome of the diaphragm was considerably below the level of articulation of the twelfth rib with the spine.

E. F., aged 39 years, had been grinding limestone for five and a half years, but had had no other exposure to dust. He had always had good health and was symptomless. Clinical and radiological examinations were quite normal.

Composition of Limestones

Limestones vary widely regarding the amount of calcium carbonate present, and many contain considerable quantities of other substances. A high calcium carbonate content is not, of course, essential for limestones used in the building industry, for roadstone, or for the manufacture of rock wool. For agricultural and chemical purposes, however, it is not economic to work low-grade limestones, and for stone dusting in mines only limestones with a low silica content should be used. Forbes and his colleagues (1950) say that they have confidential information that some coal-mining companies (presumably in America) " have had difficulty with employees engaged in the rock-dusting work ; these have complained that breathing the large quantity of fine rock dust (90% or more limestone and usually less than 5% silica) has caused serious illness ". Beal, Griffin, and Nagelschmidt (1953) analysed 30 samples of limestone used for stone dusting in mines, and found that the quartz content was less than 3% in 26, between 3 and 20% in three, and over 60% in the remaining sample which was probably sent in error. They suggest that limestones used for stone-dusting should be restricted to those with less than 3% of quartz, or 5% of total silica, and point out that legislation exists in certain countries, notably Australia, Germany, and Holland, to prevent the use of unsuitable materials for this purpose.

The particular limestone handled at this grinding factory comes from an outcrop of a bed of the Lower Limestone Group of the Carboniferous Limestone Series. The thickness of the seam is about 20 ft., and the overburden is slight. According to Simpson (1943) it is an excellent quality limestone, pale grey with occasional bands of darker stone. It is not burned for lime but used for agricultural purposes in the raw ground state, for stone dusting in mines, for poultry grit, and for road chips. He gives as a typical analysis :—

CaO	51·44%
CO_2	40·62%
SiO_2	4·93%

with amounts of Al_2O_3, Fe_2O_3, MgO, H_2O, MnO, and FeS_2 all between 0·1 and 0·9% and Na_2O, K_2O, TiO_2, and P_2O_5 less than 0·1% The amount of silica recorded represents total silica. This varies considerably and is often higher than that quoted. The results of analyses of three samples of this limestone taken recently at different times were as follows :—

	Sample 1	Sample 2	Sample 3
Total silica	11·8%	—	—
Acid insoluble material ..	—	9·6%	20·8%
Free silica	1·8%	5·1%	11·5%

Three Cases in Miners

Since discovering these cases in grinders, I have discussed the condition with doctors in various localities where limestone is worked, and have obtained information of three further cases of pneumoconiosis, one of which had proved fatal. The three men affected had been limestone-miners, the limestone they worked being of a different seam and in a different locality from that worked by the aforementioned grinders.

Case 6.—W. P. was aged 65 years at death. From the age of 12 to 32 he worked in a limestone quarry, then

FIG. 7.—Case 6 in February, 1945, aged 63 years; limestone-miner and quarryman for 39 years.

until the age of 41 in a coal-mine, chiefly as a repairer, and for the following 19 years as a limestone-miner, leaving this work at the age of 60 because of dyspnoea. After two years as a munitions storekeeper he finally gave up work. His exposure to dust was therefore 39 years as a limestone worker and nine years as a coal-miner.

He had had good health until the onset of dyspnoea about the age of 55. At the medical examination two years before his death he was found to be thin, pale, of poor musculature, and suffering from dyspnoea, cough, and expectoration, chest expansion was diminished, the respiratory murmur harsh and high-pitched, the arteries were thickened and tortuous, and there was cardiac arrhythmia. *X*-ray examination showed normal skeletal and heart shadows, the mediastinum considerably broadened, adhesions of the right dome of the diaphragm, extensive dense opacities in both lungs mainly in the outer peripheral zones, and marked translucency at the bases. The opacities were not entirely homogeneous but could be seen to have a nodular basis, and nodules of varying sizes were seen elsewhere throughout the lung fields. The appearance (Fig. 7) was that of very advanced silicosis with massive shadows, category (3)D.

Necropsy confirmed the presence of silicosis.

The following description of the pleurae and lungs has been taken from the necropsy report :—

Pleurae.—Both pleural sacs contained about 100 ml. of clear, yellow fluid. Extensive and firm fibrous adhesions bound parietal and visceral pleurae together at the apex of the left lung and over the antero-lateral surface of the right upper lobe. The interlobar fissures of the right lung were obliterated almost completely by fibrous adhesions.

Lungs.—Both lungs (R. 1,500 g., L. 1,200 g.) were large, voluminous, and showed well marked emphysematous bullae especially along the lower part of the anterior borders, their inferior borders, and on their diaphragmatic surfaces. They were dark in colour but anthracosis was not marked.

The upper lobe, most of the middle lobe, and the upper two-thirds of the lower lobe of the right lung were consolidated. The lung tissues in these areas had the consistency of tough indiarubber. A small area at the right apex and another in the lower third of the lower lobe were much less firm, and small firm nodules some 2 to 3 mm. in diameter could be felt beneath the pleura and in the parenchyma. The lung was sectioned with some difficulty owing to the fibrotic nature of the tissue, and the consolidation was seen to be due to the confluence of countless grey, fibrous, silicotic nodules giving the lung a dark, slate-grey colour. A little mucopus exuded from the smaller bronchi, but there was no evidence of tuberculosis, bronchopneumonia or bronchiectasis to the naked eye. The left lung showed similar features, but the consolidation was less extensive, involving the lower part of the upper lobe and the upper two-thirds of the lower lobe. A white fibrotic scar was seen situated subpleurally in the interlobar fissure near the apex of the lower lobe. Section revealed marked involvement of the whole lung by silicosis, with confluence of the nodules in the areas indicated. There was no evidence of tuberculosis.

The mediastinal glands were not enlarged.

Heart (report abridged).—The right ventricle showed marked hypertrophy and dilatation; the myocardium showed no evidence of recent or old infarction and the coronary vessels no atheroma.

Histology.—Sections taken from the consolidated portions of the lung show complete replacement of the normal lung parenchyma by confluent, dense, and in places, hyaline, fibrotic tissue nodules characteristic of advanced silicosis. Accompanying these changes is a moderate degree of anthracosis. Many of the arteries and arterioles show well marked endarteritis.

Sections taken from the unconsolidated lung show scattered silicotic nodules of various sizes, having a perivascular and peribronchial arrangement, lying in lung tissue which shows well marked emphysema. The alveolar capillaries are congested, and most of the alveoli contain a variable number of mononuclear cells containing both carbon and silica * particles. The walls of the smaller bronchi and bronchioles are acutely inflamed, and their lumen filled with an inflammatory exudate which contains a high fibrin content. The aveoli in their immediate neighbourhood also contain inflammatory exudate, the appearance being that of acute bronchitis and bronchiolitis with early terminal bronchopneumonia (Figs. 8 and 9).

* Seven years had elapsed since this death occurred and I have not found it possible to ascertain how the particles were identified as silica. It does not seem that micro-incineration was carried out.

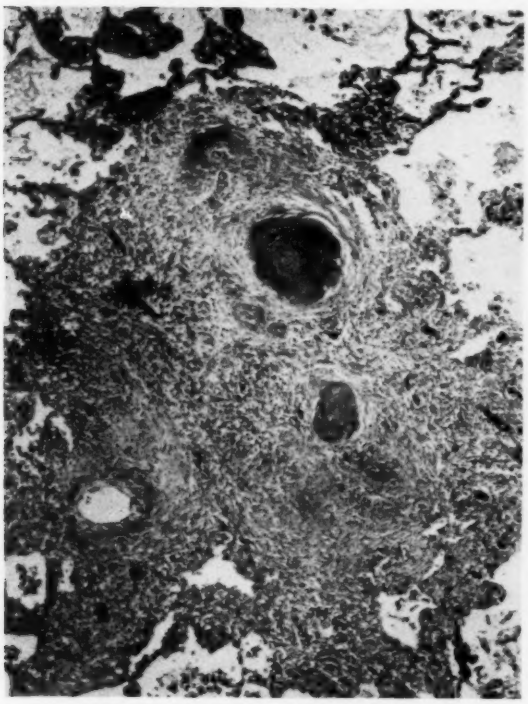

FIG. 8.—Case 6 : confluent silicotic nodules. × 30.

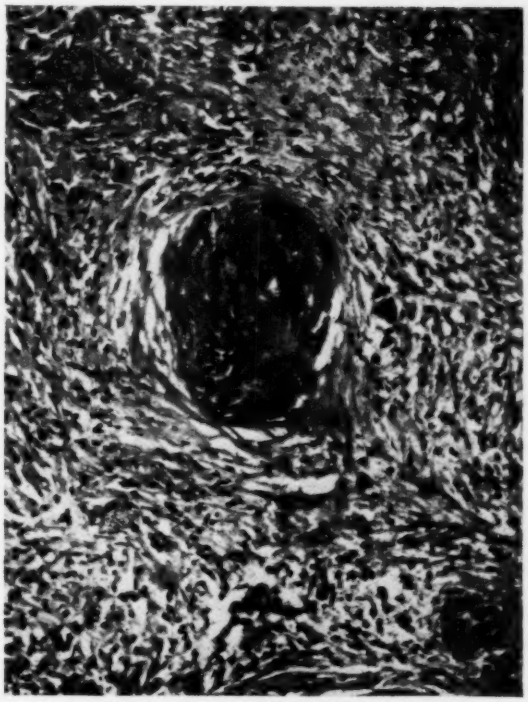

FIG. 9.—Case 6 : silicotic nodule. × 140.

Case 7.—J. L., aged 47 years, had been a gardener's boy and van boy for three years, carting limestone rock and rubble in a quarry two years, a limestone-miner for 23 years, a colliery surface worker for six months, and a coal-miner for six months. He had always had excellent health apart from pneumonia at the age of 14 years. He had pain in the left side of the chest in 1946, thought to be muscular in origin, and was not radiographed. Dyspnoea began to be noticed about 1946 ; in 1948 he resigned from a military pipe band because of breathlessness when playing bagpipes. Dyspnoea increased and slight cough and sputum appeared. Examination showed him to be a well built man of excellent musculature and of good colour. There was no finger clubbing. The chest was symmetrical, expansion 2 in., the percussion note normal, and auscultation revealed only a few sibilant rhonchi at the right base on deep inspiration. The heart was normal, there was no adenopathy, and the nasal passages were clear.

Radiographs showed a normal skeleton, heart, and diaphragm, and bilateral nodulation in both lungs principally in the upper two-thirds affecting mainly the periphery and showing a tendency to coalesce, category 3. The Pneumoconiosis Medical Panel of the Ministry of National Insurance confirmed the diagnosis of pneumoconiosis and the presence of disability which they assessed at 20% (Fig. 10).

Case 8.—A. L., aged 69 years, the father of Case 7, after spending five years as a grocer's assistant and two years on road repairs, had been a coal-miner working underground for seven years. After three years in the Army (1915–18) he became a limestone-miner, spending 36 years at this work and a further two years grinding limestone rock. He retired in November, 1951, because of ill-health which had been developing for about 10 years. His first and main symptom was dyspnoea. In the last few years, in addition to bringing on breathlessness, exertion led to syncopal attacks with loss of consciousness. Other symptoms consisted of cough, sputum, and chest pain over the lower sternum and both lung bases anteriorly. His previous health had always been good. Examination showed him to be rather corpulent and pale ; he had no finger clubbing and no cyanosis ; he had obvious dyspnoea when walking on the level but no dyspnoea at rest. Chest expansion was 1½ in. The percussion note was slightly hyper-resonant anteriorly, and breath sounds were normal but with numerous medium fine crepitations at both bases persisting after cough. Heart sounds were normal but the rate was very irregular in time and force. No other significant abnormalities were found.

An *x*-ray film taken on February 12, 1951, showed a normal skeletal shadow, a heart much enlarged to the right, and the left diaphragm raised. Throughout both lung fields there were multiple, fairly dense, soft-edged shadows differing in size and tending to confluence at the left base. The appearance (Fig. 11) was very suggestive of advanced simple pneumoconiosis of category 3 with considerable cardiac enlargement. He, also, had been granted a certificate by the Pneumoconiosis Medical

FIG. 10.—Case 7 in November, 1951, aged 47 years; limestone-miner and quarryman for 25 years.

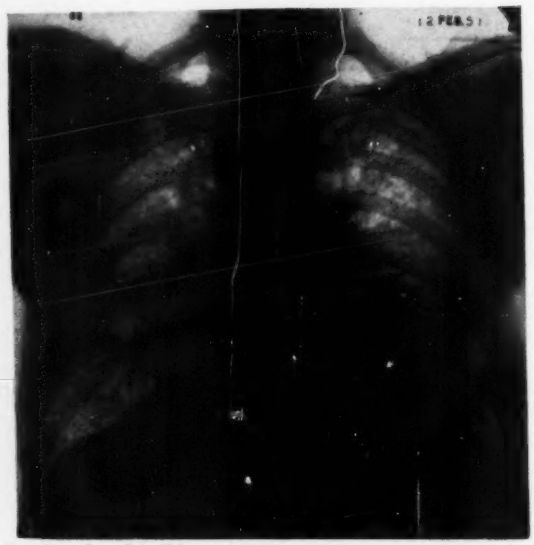

FIG. 11.—Case 8 in February, 1951, aged 69 years; limestone-miner for 36 years and grinder for two years.

Panel on account of pneumoconiosis with disability from that disease rated at 60%.

These three miners all worked in the same limestone mine. This limestone, like that to which the grinders were exposed, forms a bed of the Lower Limestone Group of the Carboniferous Limestone Series. Its thickness is about 50 ft. but the upper 30 ft., being more impure than the lower 20 ft., is not extracted. This lower portion is a dark grey, fossiliferous limestone of uniformly high quality, yielding on analysis 94·09% calcium carbonate, 1·95% magnesium carbonate, and 2·53% of insoluble residue (Robertson, Simpson, and Anderson, 1949). Much of it is used to make lime for agricultural and building purposes. Ground limestone is also produced, some of which is used for stone-dusting in coal-mines.

Recent samples, however, indicate much greater amounts of silica.

	Sample 1		Sample 2	Sample 3
	Top Stone	Bottom Stone		
Total silica (%)	14·1	7·1	—	—
Hard free silica (quartz) (%)	11·9	6·0	—	—
Acid-insoluble material (%)	—	—	12·1	9·3
Quartz (%)	—	—	6·2	3·9

The main details of the cases are summarized in Tables 1 and 2.

Discussion

Eight cases of pneumoconiosis in limestone workers are described, five in grinders and three in miners. The grinders were aged between 41 and 58 years and had been employed in this work for periods of from 16 to 28 years, the mean being 21·6 years. The miners were aged 46 to 69 years and had 25, 38, and 39 years' exposure to limestone dust. Taking the grinders and miners together, the mean duration of employment of the eight cases was 26·1 years.

There does not seem to be the slightest doubt that the pneumoconiosis has been produced by limestone dust. Three of the men, Cases 2, 4, and 7, had no history of exposure to any industrial dust other than limestone, and in one other, Case 1, such exposure amounted only to six months as a whinstone quarryman. In all the remaining cases the exposure to limestone was considerably in excess of exposures to other dusts, which exposures would have been unlikely, by themselves, to have given rise to the degree of pneumoconiosis which existed in the particular persons affected.

Three of the limestone grinders had no obvious disability; of the remaining five pneumoconiosis cases, three were partially disabled, one was totally disabled, and one had died of the disease. Symptoms were slight or absent in those who were not disabled; in the others, dyspnoea was the most prominent symptom and cough and sputum were also present. *X*-ray findings were variable; large, massive shadows were present in the fatal case, nodulation in three, reticulo-nodulation in two, and reticulation with diminished translucency and fluffy shadows in the remaining two cases. In the fatal

TABLE 1

LIMESTONE WORKERS WITH PNEUMOCONIOSIS

Case	Age	Exposure to Limestone		Other Dusty Work		Symptoms	Clinical Signs	*X*-ray Appearance and Category	Disability or Death
		Occupation	Total Duration (Years)	Occupation	Duration (Years)				
1	52	Grinding	26	Whinstone	½	Dyspnoea ++, cough, sputum	Expansion 1¾ in. Hyper-resonant Crepitations both bases. Arteriosclerosis	Nodulation (3)A	Totally disabled
2	50	Quarry 3 / Grinding 17 yrs.	20	None	—	Cough, sputum, dyspnoea, loss of weight and energy	Expansion 2½ in. crepitations R. base	Massive shadows with ground-glass appearance and stippling (3)C	Partially (40%) disabled
3	58	Grinding	28	Brickworks kiln drawer	14	Occasional cough	Expansion 1¾ in. P.n. flattened and V.R. diminished R. base	Reticulation and fluffy shadows (3)A	None
4	41	Grinding	18	None	—	Occasional cough	Expansion 2½ in. Nil abnormal	Reticulo-nodulation 2	None
5	48	Grinding	16	Whinstone / Ironstone	5 / ½	None	Expansion 2 in. Nil abnormal	Reticulo-nodulation 3	None
6	65	Quarry 20 / Miner 19 yrs.	39	Coal-mine	9	Dyspnoea ++, cough, sputum, loss of weight, etc.	Expansion diminished ; harsh high-pitched r.m.; arteriosclerosis	Massive shadows, nodulation, and emphysema (3)D	Death. Necropsy confirmation
7	47	Miner 23 / Quarry 2 yrs.	25	None	—	Dyspnoea, cough, sputum, asthmatic attacks ; occasional pain	Expansion 2 in. Normal except for few rhonchi	Nodulation 3	Partially (20%) disabled
8	69	Miner 36 / Grinding 2 yrs.	38	Coal-mine	7	Dyspnoea ; angina of effort ; syncopal attacks ; cough, sputum ; pain	Expansion 1½ in. Hyper-resonant p.n., numerous crepitations	Nodulation 3	Partially (60%) disabled

TABLE 2

LIMESTONE WORKERS WITHOUT PNEUMOCONIOSIS

Initials	Age	Exposure to Limestone		Other Dusty Work		Symptoms	Clinical Signs	Radiograph
		Occupation	Duration (Years)	Occupation	Duration (Years)			
W. L.	44	Grinding	7	Whinstone	?	Morning cough	2¾ in. expansion. Nil abnormal	Basal translucency — ? emphysema
D. B.	39	Grinding	20	None	—	None	3¼ in. expansion. Nil abnormal	Normal except increased lung markings at bases
F. G.	43	Grinding	15	Whinstone	14	Cough, occasional sputum	2½ in. expansion. Nil abnormal	Normal (diaphragm very low)
E. F.	39	Grinding	5½	None	—	None	2 in. expansion. Nil abnormal	Normal

case post-mortem examination showed extensive nodular fibrosis of the lungs.

The noxious constituent of the limestone can only be (*a*) the calcium carbonate, (*b*) the free silica, (*c*) the combined silica or silicates, or (*d*) one of the other constituents. The main constituent is calcium carbonate but there seems absolutely no evidence that this could produce pulmonary fibrosis. Silicates are present in varying amounts up to 10% in the samples analysed and must be considered as possible aetiological factors. Professor George, of Glasgow University, has suggested that acicular crystals of clay materials may exist in the limestone and might act like asbestos fibres. This is an interesting theory, and the role of silicates in producing limestone pneumoconiosis seems worthy of further inquiry, being closely associated with the question of silicatosis due to other dusts. At present, however, I consider that any action that the silicates in limestone might have in producing fibrosis of the lungs must be subordinate to that of free silica. In fact, in some cases at least the lesion seems to be a classical silicosis. Histological examination of sections of the lungs in the fatal case shows lesions composed of dense fibrous tissue with a typical whorled appearance, very suggestive of the action of silica alone unmodified by other dusts. In certain cases, notably Cases 1, 7, and 8, the *x*-ray

appearance of discrete nodulation suggests a silicotic lesion. On the other hand, the rather atypical appearance of the *x*-ray film of the patient in Case 2, who had no exposure to other dust, suggests that in some cases the lesion may not be a " pure " silicosis but may be a modified silicosis or mixed-dust pneumoconiosis. The *x*-ray appearance of the lungs of Case 3 was also suggestive of a modified lesion, but this man, in addition to 28 years' exposure to limestone dust, had had 14 years' exposure to fireclay dust, so that in his case the modifying influence may have been external to the limestone.

Exposure to limestone dust, in certain processes at least, carries a definite risk of pneumoconiosis. The severity of the risk, shown by the occurrence of five cases in a group of nine limestone grinders with more than five years' experience, and by the comparatively short period of exposure of the affected men (average 21·6 years), appears to be rather astonishing in view of the low quartz content of the material. Such an exposure period would seem to indicate a degree of risk comparable to that of many workers exposed to much more highly siliceous dusts, for instance sandstone dressers and steel fettlers. It is surprising, too, that so little information about the condition occurs in the literature. In comparison, for example, with the granite industry (granite has a quartz content of 15 to 35%), the risk of silicosis is well known, but Mair (1951), in an examination of 518 workers exposed to a dust hazard in granite dressing, found that to produce the minimum degree of radiological change, an average of 32 " dust years " was necessary, while reticulation required 38, nodulation 40, and massive shadows 42 years. In limestone mining, too, the risk would appear to be almost as great as in grinding, but I cannot estimate the incidence having no knowledge of the number of men at risk. The explanation lies almost certainly in the extremely heavy concentration of the dust cloud to which the limestone workers have been exposed.

Incidentally the view is held in some quarters that calcium carbonate dust has a beneficial action on quartz, decreasing its toxicity. The findings of Gardner (1938) have already been mentioned. Landwehr (1947) states that the higher the calcium content, the less dangerous is the rock, and Forbes and his colleagues (1950) refer to the possibility that dusts of calcium minerals may belong to the so-called " protector " dusts. The occurrence of these cases of silicosis as a result of exposure to dust containing between 1·8 and 12·1% of free silica and 85 to 95% of calcium carbonate would not appear to indicate any inhibitory effect of the latter material.

Summary

Attention is drawn to the occurrence of cases of pneumoconiosis in limestone workers.

This pneumoconiosis is associated with fibrosis of the lungs and, in advanced cases, with disability.

The lesion produced is almost certainly silicosis, due to the free silica content of the limestone.

The pneumoconiosis hazard, in the mining and grinding of at least certain limestones, is considerable, in spite of the relatively low free-silica content.

Whether or not calcium carbonate can modify the action of silica, it would not appear, judging from these observations, to have any inhibitory effect.

I am greatly indebted to many colleagues for help in my inquiries. In particular, acknowledgments are due to Dr. A. K. Turnbull for drawing my attention to Case 1, to Professor Drennan and Dr. A. D. Bain for copies of the pathological reports and photomicrographs of Case 6, to Dr. J. Simpson for the loan of the *x*-ray film of Case 6, to Dr. H. W. O. Frew for carrying out the *x*-ray examination of the grinders, to Dr. James Innes for drawing my attention to Case 7, to Dr. L. W. Laurenson for information and permission to examine Cases 7 and 8, to Dr. W. S. Shearer for the loan of the *x*-ray films of Cases 7 and 8, to Professor George for many useful suggestions and for reviewing my notes on the geology of limestones, to Dr. G. Nagelschmidt and the Government Chemist for permission to use the results of their analyses of samples of limestone, to Dr. A. Meiklejohn and Dr. J. Black for helpful criticism and advice, and to Dr. E. R. A. Merewether for his stimulating interest.

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AN EPIDEMIOLOGICAL STUDY OF BYSSINOSIS AMONG LANCASHIRE COTTON WORKERS

BY

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Raw cotton is brought to the Lancashire spinning mills in tightly compressed bales. The bales are opened and teased out in the cotton-room. The cotton is then conveyed to the blow-room where some of the dirt and short fibres are removed. In the card-room the cotton is combed by the wire teeth of the carding engines and passed through a series of machines called combers,* draw, slubbing, intermediate, and roving frames which draw it out into a thin strand (" roving ") ready for spinning.

These preparatory processes are dusty and give rise to a respiratory disease called byssinosis. All men who work in the cotton- and blow-rooms are exposed to dust, but the strippers and grinders who clean and sharpen the teeth of the carding engines are probably most exposed. The carder (foreman), the under-carder, the card setter and fitter, and the women " tenters " who mind the various machines in the card-room do not do very dusty work but are exposed to dust emitted from the carding engines. All who work in these rooms come within the provisions of the byssinosis compensation scheme. The spinners, working in the mule- and ring-rooms, which are not very dusty, are not eligible for compensation.

The disease has a characteristic history. At first the worker notices tightness of the chest and breathlessness on Mondays or on the first day back at work after an absence. On the next day he has recovered completely. These symptoms may get worse and occur on Tuesdays and then on all working days. Eventually there is severe and permanent disability.

Greenhow (1861) and Leach (1863) described the disease nearly a hundred years ago and emphasized its serious effects on the health of card-room workers. But the first measurement of its effects was given by the Registrar-General in his report for 1910–12 (published in 1923), when the death rates for strippers and grinders were given separately from other cotton workers and showed a considerable excess from respiratory disease. Collis (1909) examined 126 strippers and grinders from mills in Blackburn and found that nearly three-quarters of them were suffering from an asthmatic condition due to the inhalation of dust. Bradford Hill's statistical study of sickness among cotton workers in the period 1923–27 confirmed that strippers and grinders over 30 and female card-room workers over 25 years of age suffered excessively from respiratory disease but the excess was less for the women than for the men (Bradford Hill, 1930).

After 1920 many mills attempted with some success to reduce dust in card-rooms. Stripping brushes for cleaning the teeth of carding engines were enclosed and exhausted, carding engines vacuum cleaned, and card-rooms air-conditioned. The Departmental Committee on Dust in Card-rooms (Home Office, 1932) concluded from medical and other evidence that although some ill-health was still caused by the dust, it was not so marked since these improvements had been made.

The Departmental Committee on Compensation for Card-Room Workers (Home Office, 1939) found that in 1935–36 male card-, blow-, and cotton-room workers still suffered from an excess of respiratory sickness compared with spinners and weavers ; but the excess among the card-room workers appeared to be less than that reported earlier by Bradford Hill. On the recommendation of this committee a compensation scheme for byssinosis was started in 1940 for totally incapacitated men who had worked for at least 20 years in the dusty rooms. The scheme now includes women, and pensions are payable for disabilities assessed at 50% and over. In the period 1951–53, 150 new pensions were granted for byssinosis (Ministry of Pensions and National Insurance, 1952, 1953, and 1954). Compensation figures are notoriously unreliable indices

*Used only in fine spinning.

of the prevalence of any industrial disease (Cochrane, 1951) and these figures certainly underestimate the prevalence of byssinosis. First, they include only seriously disabled workers. Secondly, this disease is often thought by many workers and doctors to be the "chronic bronchitis" which occurs so frequently in the general population of Lancashire (Goodman, Lane, and Rampling, 1953).

Unlike the pneumoconioses caused by mineral dusts there are no specific *x*-ray changes. The aetiology is obscure since the causative agent and its mode of action are unknown. The one recorded study of the pathology by Shaw Dunn and Sheehan (1932) does not shed any light on aetiology or help in diagnosis at necropsy, since they found chronic bronchitis and emphysema which was in no way specific in type.

It was decided first of all to find out if byssinosis is still a major problem in the Lancashire cotton industry. It was thought that it might be, since a recent study revealed that chronic chest disease overshadowed all others in middle-aged cotton workers employed in the dusty trades (Schilling, Goodman, and O'Sullivan, 1952).

The study described in this paper was made in a large group of Lancashire mills spinning the coarser grades of raw cotton. They were chosen because they are said to be dustier than mills spinning finer grades and to have a higher prevalence of byssinosis (Collis, 1909). The field work was undertaken between February and December, 1953, and between November and December, 1954. The reliability of the diagnosis in byssinosis has been investigated by Schilling, Hughes, and Dingwall-Fordyce (1955) and found to be sufficiently good to enable a reasonably accurate estimate of prevalence to be made. This paper reports the prevalence in male card- and blow-room workers, mule spinners, female card-room workers, and ring spinners; and also the severity of disability caused by the disease.

PROCEDURE

Mills and Populations Studied

In Oldham and the neighbouring towns of Shaw, Middleton, and Chadderton there are 112 mills spinning the coarser grades of raw cotton. Twenty-eight were selected as those which were most likely to cooperate.*

Men aged between 40 and 59 years in the card- and blow-rooms† were the first population studied. There was a total of 202 of these men in the 28 mills; 12 men were excluded for various reasons (Table 1) and the final analysis of results was made on 190.

TABLE 1
POPULATIONS OF MALE COTTON WORKERS AND CONTROLS AGED 40–59 YEARS

	Male Card- and Blow-room Workers	Factory Workers (Controls)
Examinations completed ..	190 (94%)	88 (88%)
Excluded :		
For chest disease (non-industrial)	2*	3†
For changed conditions of work during study ..	5	—
Left during study	—	5
Refused	5	4
Total	202	100

* One man extensive fibrosis in left upper zone. One man fibrosis right upper zone with cavity.
† One man active tuberculous lesion in right upper zone. One man pleural effusion at left base. One man extensive pleurisy.

For comparison a group of men of similar ages to the cotton workers but who had never worked in card- and blow-rooms was examined. Two engineering factories in the Oldham district provided these controls, 100 men in all consisting of the total population between 40 and 60 years from one factory, and a random sample of the total population of this age from the other. They were skilled or semi-skilled manual workers and their foremen and had not been exposed to any recognized hazard causing industrial pulmonary disease. Twelve men were excluded for various reasons (Table 1) and the final analysis was made on 88.

TABLE 2
POPULATIONS OF WOMEN CARD- AND RING-ROOM WORKERS AND MALE MULE SPINNERS, AGED 40–59, AT RISK IN 6 MILLS

	Women		Men
	Card-room Workers	Ring-room Workers	Mule Spinners
Examinations completed	218 (97%)	61 (95%)	62 (89%)
Excluded	5	2	4
Refused	3	1	4
Total	226	64	70

After these men had been seen and the results analysed, groups of women card- and ring-room workers and male mule spinners from six of the 28 mills were examined in less detail to complete the epidemiological picture of byssinosis. The populations at risk and the numbers seen are given in Table 2.

Examinations

For the male card- and blow-room workers postero-anterior radiographs of the chest in

* A random sample might well have included mills which would not have cooperated, thus causing high refusal rates. As will be seen later, there is no reason to believe that the mills visited were not representative of all the mills in the prevalence of respiratory disease.
† Cotton-room workers were not included because there are very few of them and they do not usually remain in this job for long.

inspiration and expiration and a lateral radiograph were first taken using full-sized films. Later these men were examined at their place of work on two separate occasions on working days other than Mondays and Fridays. Two examinations were made (in all but seven of the men) to determine the reliability of the signs and symptoms of byssinosis. At the first an occupational history and notes of previous illnesses were recorded and detailed questions asked about chest complaints. The chest was then examined clinically and the blood pressure recorded. At the second examination made about four months later the questions about chest complaints and the clinical examinations were repeated by the other observer who had no knowledge of the previous results except the occupational history and the record of previous illnesses.

The volume of gas expelled during the first 0·75 sec. of a forced expiration was measured by a modified Gaensler (1951) apparatus. Five readings were taken and the results calculated from the mean of the three highest (correct to B.T.P.). Tiffeneau, Bousser, and Drutel (1949) have used this test as an indirect measure of maximum breathing capacity. Kennedy (1953) called this measurement the "expiratory flow rate" (E.F.R.) and showed it correlated very highly with the maximum voluntary ventilation measured directly. We have expressed our results in litres per min. as described by Kennedy but prefer Tiffeneau's terminology (indirect M.V.V.) The close correlation between the maximum breathing capacity measured directly (at a fixed rate of breathing) and that derived indirectly from the volume of gas expelled during a single fast expiration has been confirmed by Bernstein and Kazantzis (1954).

DIAGNOSIS OF BYSSINOSIS

History

Each observer classified the men on their clinical histories as follows :

Normal :	No symptoms of chest tightness or breathlessness on Mondays
Byssinosis :	
Grade I	Chest tightness and/or breathlessness on Mondays only
Grade II	Chest tightness and/or breathlessness on Mondays and other days

Both observers examined 183 cotton workers and made the same diagnosis in 139 (76%). After consultation the diagnosis was agreed in 20 (11%) more. In six men the observers continued to disagree on the presence or absence of byssinosis (see Table 3).

Physical Signs

The disagreement between the observers on the detection of physical signs normally accepted as being associated with emphysema, such as absent apical impulse and chest fixity, was too great to add much to the precision of the diagnosis of byssinosis (Schilling, Hughes, and Dingwall-Fordyce, 1955). Thus the results of the clinical examinations of the chest are not included in this paper.

Blood pressures, which will be discussed in another paper, were not on the average significantly higher in the card- and blow-room workers than in the controls, as was found previously (Schilling and others, 1952).

Radiographs.—In a study of byssinosis 20 years ago Fletcher found changes in the lung fields consistent with chronic bronchitis and some degree of emphysema, but he thought that there was some excess of the root and bronchial shadows of a degree not seen in ordinary bronchitis (Prausnitz, 1936). In our study the radiographs of three samples of 15 men each were chosen : cotton workers with Grade II byssinosis, normal cotton workers, and normal controls. All were matched for age and no one with a history of another respiratory disease was included. These films were studied by one of the authors (J. C. G.) with Dr. A. L. Cochrane. Although these readers knew from which group the films came they were unable to detect any striking differences between them. Thus radiographs did not assist in diagnosis. The only difference noted was a smaller excursion of the diaphragm on comparing inspiratory and expiratory films. The average excursion of the byssinotics was 3·28 cm. compared with 4·55 cm. for the other two groups together. The difference is significant at the 2% level.

The diagnosis of byssinosis, therefore, depended on the worker's account of his symptoms. It would have been preferable if the diagnosis had been made without the observer knowing the man's occupation in the mill but this was rarely possible because discussion of his symptoms usually revealed where he worked. The consistency of the histories and the agreement between the gradings of byssinosis and the test of ventilatory capacity (discussed later) are evidence in support of the reliability of the assessments. The discovery of cases of byssinosis in ring-room workers and mule spinners where it was not expected suggests that the results are not biased towards an over-estimate of its prevalence elsewhere.

Chronic bronchitis was diagnosed on a history of persistent cough with sputum in the absence of other respiratory disease. The inter-observer reliability

was not measured, as cases were diagnosed only after joint discussion of the histories obtained by both observers.

RESULTS

MALE CARD- AND BLOW-ROOM WORKERS

Altogether 115 (60%) of the male card- and blow-room workers gave a clinical history of byssinosis (Table 3). In 24 men in whom the observers failed to agree on the diagnosis of byssinosis the less favourable diagnosis was chosen.

TABLE 3
PREVALENCE OF BYSSINOSIS IN 190 MALE CARD- AND BLOW-ROOM WORKERS

	Observers Agreed		Observers Disagreed	Examined Once	Total
	Initially	After Consultation			
Normal ..	72	1	—	2	75 (39%)
Grade I Byssinosis	47	11	6	3	67 (35%)
Grade II Byssinosis	20	8	18	2	48 (25%)
Total ..	139	20	24	7	190

A typical case history for each grade of byssinosis is given in Appendix I.

Among the men graded as normal there were 15 who told both observers that they had noticed other symptoms, particularly on Mondays. These symptoms and the number of times they were recorded were : cough (8) ; irritation of respiratory tract by smoke (5) ; breathing more difficult on Monday but not amounting to tightness (2) ; headache (1) ; feeling feverish (1) ; and fatigue (1). These symptoms appear to be early or mild manifestations of the disease. Among the 88 controls none complained of tightness of the chest or breathlessness on Mondays ; one of the 12 men diagnosed as having chronic bronchitis told one observer that his breathing was worse on Mondays.

Occupation

By allocating men to the occupation in which they had spent more than 50% of their time it was possible to compare the prevalence of disease in four groups : (1) Carders and under-carders ; (2) card setters and fitters, cotton-room men,* and men with a mixed occupational history ; (3) strippers and grinders ; (4) blow-room workers.

Table 4 shows that 65% of the strippers and grinders and the blow-room workers had byssinosis and 42% of the carders and under-carders and the others were affected. This supports the view that the strippers and grinders and blow-room workers are exposed to more dust than the other men in the card-room.

Disability by Clinical Assessment

Respiratory disability was first assessed on the clinical grading of dyspnoea.

Since breathlessness which varies from day to day is a characteristic feature of byssinosis, it was graded for the men's best and worst days as follows :

Normal I : Able to keep up with normal men of own age on hills.
Slight II : Only able to keep up with normal men of own age on the level.
Moderate III : Unable to do the above but can walk about a mile at own speed without stopping.
Severe IV : Only able to walk about a hundred yards without stopping.
„ *V* : Unable to do the above.

Table 5 shows that the cotton workers have more temporary and permanent effort intolerance than the controls; the strippers and grinders and blow-room workers (Group B) having more than the other cotton workers (Group A).

Disability by Spirometric Assessment

As the assessment of respiratory disability by dyspnoea grading is liable to a relatively large observer error (Schilling and others, 1955), the results of the more objective maximum voluntary ventilation measurement are of interest. Like other

* These men, although now employed in card- and blow-rooms, have been allocated to the cotton-room because they had spent more than 50% of their time there.

TABLE 4
PREVALENCE OF BYSSINOSIS IN VARIOUS OCCUPATIONS IN CARD- AND BLOW-ROOMS

Group		Number	Mean Age	Mean Exposure (years)	Normal	Byssinosis		Percentage Affected
						I	II	
Carders and U/carders	A	21	48·6	23·2	12	5	4	42·5%
Others *	A	19	47·1	23·2	11	5	3	
Strippers and grinders	B	112	48·7	22·8	39	46	27	65·3%
Blow-room	B	38	50·6	25·9	13	11	14	

* 10 card setters and fitters, 6 cotton-room men, 3 mixed.
Proportionately more blow-room workers than strippers and grinders were seriously affected, perhaps because they were on the average older men with longer exposures.

TABLE 5

DYSPNOEA GRADINGS AMONG 186 MALE COTTON WORKERS AND 88 CONTROLS

Dyspnoea Grading	On Best Days (Permanent Disability)			On Worst Days (Temporary Disability)		
	Controls 88	Group A 39	Group B 147	Controls 88	Group A 39	Group B 147
Normal I	90%	82%	63%	85%	65%	49%
Slight II	10%	13%	28%	14%	18%	22%
Moderate III	—	5%	8%	1%	10%	19%
Severe IV	—	—	1%	—	6%	9%
" V	—	—	—	—	—	2%
Excluded *	—	1	3	—	1	3

* Four cotton workers were excluded for the following reasons : Arthrodesis left knee, intermittent claudication, ? carcinoma of stomach, mitral incompetence.

The observers agreed exactly in their gradings on the best days for 65% of cotton workers and 88% of the controls. The corresponding figures for the worst days were 58% and 88%. Where there was a disagreement the mean of the observers' gradings was taken. Of the men who had grades of 2½, 3½, and 4½ half were allocated to the higher and half to the lower grade.

physiological tests it demands cooperation from the subject but in this study cooperation was, almost without exception, excellent. This is supported by the close repeatability of values obtained on the same subjects in these factories and mills over a period of several months, using more than one observer. The standard error of an estimate of the maximum voluntary ventilation was 6·3 l./min. Figure 1 and Table 6 show that the cotton workers without byssinosis, age for age, have an average M.V.V. very similar to that of the controls. Men with Grade II byssinosis have average values lower than men with Grade I byssinosis. Also, men with Grade I byssinosis have average values significantly lower than normal. This is of interest since these men complained of breathlessness on Mondays only and all the tests were done on other days.

Since all the cotton workers were working they were a selected population, those with severe byssinosis or other illnesses having been obliged to leave the trade. Such a process of selection probably explains the relatively high M.V.V. of the older men with byssinosis. Eight men receiving disability pensions for byssinosis but not belonging to this group were found to have a low M.V.V.* Of the 12 controls with bronchitis, eight had lower values than the normal men, but some did not complain of any effort intolerance.

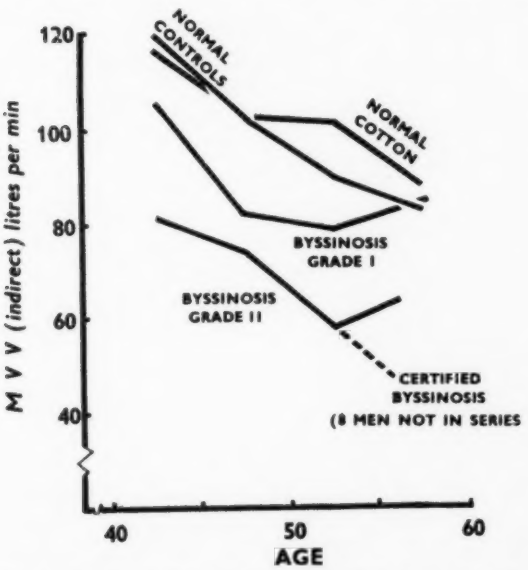

FIG. 1.—The timed vital capacity expressed as "indirect" M.V.V. (l./min.) in cotton workers and normal controls, and eight men certified as suffering from byssinosis and not working. (These differences between men with byssinosis and normals could be due to these groups being anthropometrically different. This is very unlikely since their mean chest circumferences (in expiration) were almost identical.)

TABLE 6

TIMED VITAL CAPACITIES EXPRESSED AS MAXIMUM VOLUNTARY VENTILATION (INDIRECT) IN LITRES/MIN. OF COTTON WORKERS AND CONTROLS

Age		Cotton Workers			Controls	
		Normal	Grade I	Grade II	Normal	Bronchitis
40–44	Mean	117†	106†	11	121	105/124
	S.D.	20·1	18·9	30	21·8	
	No.	27	16	12	31	2
45–49	Mean	103*	82*	74	103	67/115
	S.D.	19·1	29·2	21·5	25·1	
	No.	22	22	11	15	2
50–54	Mean	102†	7?*†	58*	90	78/80
	S.D.	22·5	26·9	26·3	19·8	
	No.	9	18	14	17	2
55–59	Mean	88†	85	66†	83	64
	S.D.	16·4	20·2	26·0	14·3	28·8
	No.	15	10	11	9	6

Three cotton workers and four controls were not available for this test.

* Significant difference $P<0.01$.

† Significant difference $P<0.05$.

* The mean age of these men was 55·9, and their mean M.V.V. was 47·3 l./min. (see Fig. 1).

A pilot study had shown that the results of this test differed on Monday from other days of the week but not between other days within the same week. After the main investigation the extent of the temporary disability on Mondays was assessed by measuring the M.V.V. of 46 cotton workers and 24 controls twice, first on a Thursday and then on the following Monday. The two groups with byssinosis show a highly significant reduction in M.V.V. on Mondays (Table 7 and Fig. 2), although the change in absolute values is not large. The normal cotton workers and the controls showed no significant change between Monday and Thursday.

TABLE 7

PROPORTIONAL CHANGE IN MAXIMUM VOLUNTARY VENTILATION (INDIRECT) ON MONDAYS

Group	No. of Men	Mean of M.V.V.s (l./min.) on Mon./Thurs. × 100	S.E. of Mean	Significance of Proportional Decrease on Monday
Controls ..	24	100%	1·1	—
Cotton workers normal ..	13	97%	2·1	P=0·1 (t=1·3)
Grade I byssinosis ..	22	91%	2·1	P<0·0005(t=4·0)
Grade II byssinosis ..	11	90%	2·0	P<0·0005(t=4·7)

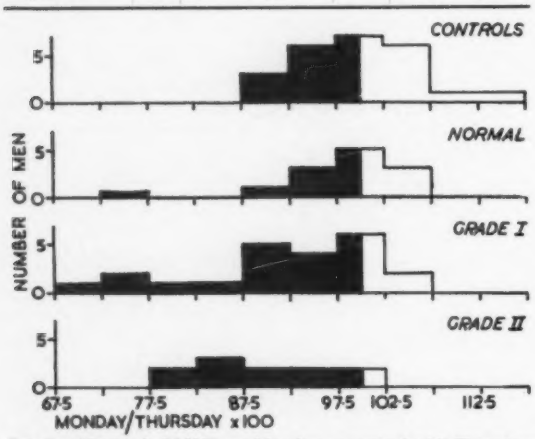

FIG. 2.—Change in M.V.V. on Mondays compared with Thursdays.

The Severely Disabled Men

Thirteen cotton workers were considered to be seriously disabled because of the severity of their Monday symptoms and dyspnoea on their best days. All but two of them had an M.V.V. below the means for their ages (Table 8).

A maximum voluntary ventilation of less than 50 l./min. indicates quite severe respiratory disability in men of this age. There were 13 cotton workers, excluding the five in Table 8, who had byssinosis and an M.V.V. of less than 50 l./min. Four controls (three with bronchitis) also had M.V.V.s below this level.

TABLE 8

COTTON WORKERS SEVERELY DISABLED WITH BYSSINOSIS (GRADE II)

Patient	Mean Grade Dyspnoea on Best Days	M.V.V. (l./min.)		Exposure to Cotton (years)	Occupation
		Observed	Expected†		
M.G.*	4	39	80	39	Stripper and grinder
H.H.*	3·5	87	70	30	Blow-room
C.J.	3·5	24	80	28	Stripper and grinder
H.B.*	3	78	89	35	Card-room
B.L.*	3	75	87	31	Stripper and grinder
D.V.	3	72	89	30	Stripper and grinder
F.M.*	3	25	87	27	Blow-room
S.J.*	3	36	94	29	Blow-room
C.H.	3	82	70	35	Stripper and grinder
R.F.	2·5	51	80	38	Stripper and grinder
B.T.*	2·5	81	97	21	Stripper and grinder
W.G.*	2·5	29	78	34	Blow-room
E.J.	2·5	82	113	21	Under-carder

* These men have since been awarded a 50% disability pension for byssinosis.

† The expected M.V.V. in which an allowance is made for age was calculated from the regression equation, $y = 210{\cdot}8 - 2{\cdot}4x$ for all cotton workers and controls, where y = M.V.V. and x = age.

Altogether there were 26 cotton workers severely disabled with byssinosis; and there were 12 other men not yet seriously disabled who told both observers that their symptoms of byssinosis had definitely got worse during the last 12 months.

Length of Exposure

Table 9 shows that the prevalence of the disease among the men who have been in the industry at least 20 years is more than twice as high as it is among those who have been in less than 10 years.

TABLE 9

PREVALENCE OF BYSSINOSIS AND LENGTH OF EXPOSURE IN CARD- AND BLOW-ROOMS

Years of Exposure	Normal	Byssinotics		
		Grade I	Grade II	Total (%)
0– 9	14	4	3	33
10–19	22	18	7	53
20–29	22	22	19	65
30+	17	23	19	71

But these figures take no account of the men who have left the industry because of the disease and, therefore, underestimate its true prevalence in relation to exposure. With age * held constant there is no correlation ($r = +0{\cdot}02$) between the M.V.V.s and exposure for the cotton workers.

This surprising finding cannot be adequately explained with the small groups available. We think it is probably the result of a high degree of selection

* The correlation between M.V.V. and age with exposure held constant was $r = -0{\cdot}47$.

in the population, the more disabled men with a low M.V.V. having left the mills as indicated by Fig. 1.

It may also be related to the type of response to the dust. It appears that only a proportion of subjects is susceptible at all to this dust and it may be that after a certain stage is reached the condition, and in particular the decline in ventilatory capacity, is progressive in the absence of further exposure. The stage at which this progressive decline takes place may be much more closely related to the age of the subject than to his exposure.

For the disabled men and those who were definitely getting worse, periods of exposure ranged from 18 to 39 years. All but one man, who was slightly disabled and getting worse, had worked in card- or blow-rooms for more than 20 years.

Unfortunately, the disease has such an insidious onset that it is very difficult for men to remember when their symptoms started. Thus it was not possible to calculate reliably each man's period of exposure before the onset of symptoms (induction time). But the induction times of the 58 men who gave the same answers to both observers ranged from less than one year to more than 30 years with a mean of 16·7.

Chronic Bronchitis

Men with chronic bronchitis develop tightness of the chest whenever they are exposed to a sufficient concentration of any dust. In the early stages of byssinosis the worker is affected only by cotton dust and only on Mondays. Even in the later stages of the disease Monday is the worst day, although the card-rooms are not dustier on that day (Drummond, Hamlin, Donoghue, and Brownsett, 1954).

The symptom complex of chronic bronchitis is, therefore, not the same as byssinosis.

There were two blow-room workers who had symptoms of chronic bronchitis but not of byssinosis (see Appendix I). As byssinosis progresses the patient often also has symptoms of chronic bronchitis, but it is not an invariable complication. There were 12 men with byssinosis who had a dry cough and 20 who had no cough at all. The added effect of a respiratory infection, such as bronchitis, on the progress of byssinosis will be discussed in a later paper.

Prevalence of Byssinosis in Male Card- and Blow-room Workers in Other Mills

Since the 28 mills were not a random sample of all the 112 mills in the Oldham area, it is not possible from these results alone to be certain about the general prevalence of the disease in this area. But there are two further sources of information. Seventeen other mills in the Oldham area were studied either previously or in the pilot survey of this inquiry; four mills doing coarse spinning in the Ashton-under-Lyne district have also been recently studied, but not in as great detail.

The proportions of card- and blow-room workers affected with byssinosis are similar in all three groups of mills:

Group	Total No. of Men (aged 40–59)	No. with Byssinosis		
		I	II	Total
28 mills in Oldham area ..	190	67	48	60%
17 " " " " ..	107	33	23	52%
4 " " Ashton-under-Lyne district	44	17	7	54%

It thus seems likely that the prevalence figures established for the 28 mills are reasonably representative of all mills doing coarse spinning.

THE WOMEN CARD-ROOM WORKERS AND THE SPINNERS

A similar procedure was adopted in studying the women card-room workers, but they were not examined clinically and were seen by only one observer. The M.V.V. was not measured. As byssinosis has not been reported previously among spinners, all those (with one exception) who gave a history of the disease were seen by the second observer and Professor R. E. Lane, and were examined clinically and radiographed at the Manchester Royal Infirmary. The observers discussed the case histories of all workers in whom byssinosis was diagnosed and agreed on the recorded diagnosis.

In the card-room the draw and slubber frames are close to the carding engines and the intermediate and roving frames are some distance from them. The results in Table 10 and Fig. 3 show that the prevalence of byssinosis in the card-rooms was less in the workers farther away from the carding engines, and that very few workers in the spinning rooms were affected. This epidemiological pattern was fairly consistent for each of the six mills (see Appendix II). While there is always some movement of women tenters in the card-room from job to job, there were enough card-room tenters who were known to have worked consistently on the same jobs to confirm the validity of these results.

Disability

As the M.V.V. was not measured in this group it was not possible to assess their disability with equal confidence. But there were 12 (nine working near the carding engines) who had byssinosis and moderate or severe effort intolerance on their best days. None of the ring spinners or mule spinners was thought to be seriously disabled by

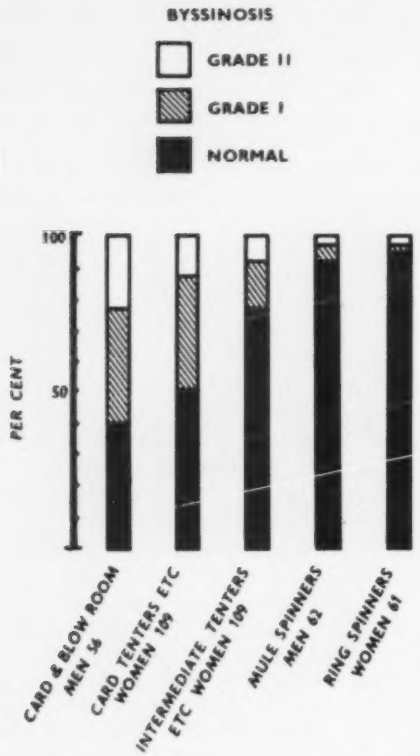

FIG. 3.—Prevalence of byssinosis in the card-room workers and spinners in the six mills.

byssinosis alone. The clinical study of the spinners will be reported in more detail elsewhere.

DISCUSSION

These results indicate that byssinosis can usually be diagnosed reliably in this type of field research. It does not follow that it can be similarly diagnosed by doctors considering claimants for compensation. A claimant cannot be expected to have the same outlook towards his disease as a participant in a survey. Doctors on medical panels may also examine those who have left the industry and are so disabled and distressed by dyspnoea that they cannot recall that they once had the characteristic Monday symptoms.

The existing compensation scheme (Ministry of National Insurance, 1948) which is now under review limits awards to those with disability assessed at 50% or more who have worked in the prescribed processes for at least 20 years. These limits, made because of the difficulty of distinguishing byssinosis from bronchitis and emphysema of non-occupational origin, may have serious consequences and cause hardship to the workman. Some of those with disabilities assessed at less than 50% either continue their dusty occupation and get worse or leave on medical advice and receive no pension. One man in the pilot survey of this study was severely disabled after 16 years in the blow-room but he had spent 20 years in the spinning room. Another with less than 20 years in the card-room was getting rapidly worse but was not yet seriously disabled.

Some of the difficulties of diagnosing byssinosis for compensation could be overcome if workers at risk were medically examined at regular intervals, as is done in some dusty trades. Such a system of medical supervision would also indicate the mills which had high attack rates of byssinosis and which needed to pay special attention to dust control.

The coal-mining industry has a scheme whereby miners with less disabling stages of pneumoconiosis are encouraged to continue working under approved conditions (Hugh-Jones and Fletcher, 1951). A similar scheme might be developed for the cotton industry. Blow-rooms and card-rooms, in which only rayon fibres are processed, could be approved immediately since byssinosis is not known to occur in them. By further research it should be possible to assess the atmospheric concentration of dust which is safe and thus enable some mills spinning raw cotton to be approved. It is also necessary to know more about the natural history of the disease

TABLE 10
PREVALENCE OF BYSSINOSIS IN CARD-ROOM WORKERS AND SPINNERS AGED 40–59 IN SIX MILLS

Group	Sex	Number	Mean Age	Mean Exposure	Clinical Condition			
					Normal	Byssinosis		
						I	II	Total (%)
Card- and blow-room workers	M.	56	48·2	24·8	21	22	13	62
Card, draw, frame, slubber tenters	F.	109	48·8	26·8	58	37	14	47
Intermediate and rover tenters	F.	109	48·4	27·3	84	17	8	23
Mule spinners	M.	62	49·6	29·0	55	5	2	11
Ring spinners	F.	61	48·2	28·2	59	1	1	3

and in particular its course in those who have had definite symptoms but who have been removed from further dust exposure.

All but three of the 28 mills studied were spinning the coarser grades of cotton * which account for 92% by weight of the yarn produced in the United Kingdom (Cotton Board, 1954). Thus they are likely as a group to be fairly typical of conditions in all cotton mills with the exception of the smaller number spinning the fine counts and in which it is thought that there is a lower prevalence of byssinosis. Accurate estimates of prevalence in relation to coarseness of cotton spun will be considered when it has been possible to investigate a full range of mills. The 28 mills in this study employed 3,933 men and 6,624 women of all ages, excluding office workers : 23·4% of the men and 33·4% of the women worked in the cotton blow- or card-rooms and were exposed to the risk of developing disabling byssinosis. There is no doubt that in spite of the active efforts to control dust, byssinosis is a major problem in the card-rooms of this type of spinning mill.

The components of card-room dust which may contain the causative agent of byssinosis are the fly, consisting of short pieces of broken fibre, fine dust derived from dried plant debris, bacteria, and moulds. Prausnitz (1936) suggested that the soluble protein fraction of the fine cotton dust was the cause of the disease. But this has not been supported by the recent work of Cayton, Furness, and Maitland (1952), who did skin testing with various extracts.

The epidemiological pattern of prevalence being inversely related to the distance of working groups from the carding engines suggests a new approach to the study of byssinosis, namely to investigate the relationship between concentrations of the various types of dust and prevalence in mills with stable populations. This study now started may help in isolating the fraction of dust causing the disease. At least it should indicate a maximum allowable concentration of dust which would give the cotton industry a target for dust suppression and would be a valuable step towards preventing byssinosis and enabling the disabled men to work under approved conditions.

SUMMARY

One hundred and ninety male card- and blow-room workers aged 40 to 59 years from 28 mills spinning the coarser grades of cotton, and 88 men of the same age from two engineering factories were examined clinically and radiologically for respiratory disease.

One hundred and fifteen (60%) of the cotton workers had symptoms of byssinosis characterized by tightness of the chest and breathlessness on Mondays. Respiratory disability was assessed by the severity of tightness of the chest and dyspnoea and the volume of gas expelled during the first 0·75 sec. of a forced expiration. Twenty-six (14%) cotton workers were seriously disabled (eight have since received disability pensions) and 12 others were not so seriously disabled but appeared to be getting progressively worse. Of the controls, only four (4·5%), three of whom had bronchitis, showed any serious degree of respiratory disability.

Subsequently, 218 women card-room workers, 61 ring spinners, and 62 mule spinners from six mills were examined in less detail than the men ; seven mule spinners and two ring spinners had symptoms of byssinosis. The prevalence of byssinosis was inversely related to the distance of workers from the carding engines. This epidemiological finding may help to isolate the fraction of dust causing the disease and to establish maximum allowable concentrations of dust in card-rooms. Of all the employees in the 28 mills, 23% of the men and 33% of the women were exposed to the risk of developing disabling byssinosis.

The clinical differences between chronic bronchitis and byssinosis are discussed. It is probable that the extent of byssinosis has been obscured by the high prevalence of chronic bronchitis in Lancashire.

We should like to thank the many employers, mill managers, welfare officers, Trade Union representatives, factory inspectors, and workers whose cooperation made this study possible. We acknowledge our gratitude to Mr. W. G. Clarke and his team who so successfully toured the mills and factories with the mobile *x*-ray van under exceptionally severe weather conditions, and to the Department of Medical Illustration at the Manchester Royal Infirmary for preparing Figs. 1 and 3. We are grateful for the help and valuable criticism we received from our colleagues. One of us (R. S. F. S.) is grateful to the Medical Research Council for a grant to study byssinosis.

* That is, counts below 56; the count is the number of hanks of 840 yd. in 1 lb. of cotton.

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APPENDIX I

Examples of the histories of men with byssinosis and chronic bronchitis are given below.

Byssinosis Grade I

Case 1.—H. W. (203), a stripper and grinder, aged 45 years, had worked in the card-room for 25 years. He gave no history of any other chest illness. At about 3 p.m. on Mondays he noticed that he was slightly short of breath and that his chest felt tight. He had little appetite on Monday evenings. His chest began to feel better at about 11 p.m. On Tuesdays and other working days he was unaffected. He first noticed these symptoms on Mondays about 15 years ago, and they were not getting any worse. The heart and chest revealed no abnormal physical signs. Blood pressure was 125/85 mm. Hg, M.V.V. 114 l./min., and radiographs normal.

Byssinosis Grade II

Case 2.—E. W. (286), a carder, aged 49 years, had worked for six years as a carder and previously for 24 years either as a blow-room worker or as a stripper and grinder. He had no history of any other chest illness. At about 10 a.m. on Mondays he felt a little tight on the chest and noticed that he was breathing slightly more quickly. He got worse as the day went on. By 4 p.m. he felt absolutely done-up and on Mondays it took him 10 minutes, which was at least twice the usual time, to walk 300 yards to his home. He had little appetite and never went out on Mondays. He felt better when he got up on Tuesday mornings, but his chest was not really normal until Thursdays. He had a dry cough which troubled him every night, except when he was on holiday. He first noticed these symptoms seven years ago. His complaint had definitely got worse in the last 12 months. His heart was normal. Coarse rhonchi were heard in the left axillary region by both observers. Blood pressure was 140/95 mm. Hg, M.V.V. 85 l./min., and radiographs normal.

Disabling Byssinosis with Less than 20 Years' Exposure

Case 3.—O. A. (2), a blow-room worker, aged 50, had worked for a total of 17 years in card- and blow-rooms. He worked in the spinning room from the age of 12 to 32 years. He gave no history of chest illness. About five years ago he noticed chest tightness and breathlessness on Mondays. He had got progressively worse and now had symptoms on every working day. He was permanently short of breath (dyspnoea grade 3). He had a dry cough. Generalized rhonchi in the chest were heard by both observers. The heart was normal and blood pressure was 125/90 mm. Hg.

Chronic Bronchitis without Byssinosis

Case 4.—G. W. (224), a blow-room man, aged 48 years, worked for 12 years in broken periods as a stripper and grinder and blow-room man. He gave a history of bronchitis, aged 20, at the time of going into the card-room, and of pneumonia when aged 32. His breathing was affected by cotton dust when he first entered the card-room. It had never been worse on a Monday than on any other day, but cotton dust, like other dusts, made him cough and wheeze. He had a cough with sputum in the summer and winter. He had some effort intolerance and generalized rhonchi in the chest. Blood pressure was 130/80 mm. Hg, M.V.V. 54 l./min., and radiographs were normal.

Case 5.—H. A. (58), a blow-room man, aged 44 years, had worked for 26 years in the cotton chamber and blow-room. He gave a history of having had bronchitis three to four years before. He had no symptoms of chest tightness on Mondays. He had an early morning cough with sputum, which was made worse when he did a dusty job such as taking the dirt out of the machine. He had no effort intolerance. Blood pressure was 144/92 mm. Hg, M.V.V. 89 l./min., and radiographs were normal.

APPENDIX II

THE PREVALENCE OF BYSSINOSIS IN ALL THE GROUPS OF WORKERS IN EACH OF THE SIX MILLS

Mill	Male Card- and Blow-room			Female Card Tenters, etc.			Intermediate Tenters, etc.			Mule Spinners			Ring Spinners		
	N	I	II	N	I	II	N	I	II	N	I	II	N	I	II
A	2	3	1	4	7	5	4	2	1	7	2	1	7	1	1
B	3	1	1	7	6	1	17	2	2	30	0	1	16	0	0
C	9	3	1	26	4	0	31	2	0	None			Not examined		
D	4	4	3	9	6	4	7	3	2	None			14	0	0
E	2	8	5	6	4	2	16	3	0	None			16	0	0
F	1	3	2	6	10	2	9	5	3	18	3	0	6	0	0
Total	21	22	13	58	37	14	84	17	8	55	5	2	59	1	1
	38%	39%	23%	53%	34%	13%	77%	16%	7%	89%	9%	3%	97%	2%	2%

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THE EFFECT OF CORTISONE ON ESTABLISHED SILICOTIC FIBROSIS IN THE LUNGS OF RATS

BY

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In man, cortisone has not been shown to have any appreciable effect on long-standing fibrosis. Kennedy, Pare, Pump, Beck, Johnson, Epstein, Venning, and Browne (1951) treated a case of pulmonary silicosis with some clinical improvement in the patient's condition, although this was not supported by the *x*-ray findings; and Kennedy (1954) has recently reported rather similar findings (subjective but no objective improvement) in pneumoconiotic potters and coal-miners.

Harrison, King, Dale, and Sichel (1952) investigated the action of cortisone on developing fibrous tissue in the lungs of rats produced by intratracheal injection of quartz particles. Cortisone appeared to interfere with the migration of dust-laden phagocytes in the lung, where they remained diffusely distributed within alveoli instead of aggregating to form discrete nodules. It also modified the development of pulmonary silicotic nodules in amount and distribution, but did not significantly alter the maturation of fibrous tissue from reticulin to collagen. Marenghi and Rota (1954), however, concluded from their experiments with cortisone treatment of quartz-dusted rats that cortisone had very little influence on the initial cellular reaction, but that it delayed or prevented the transformation of reticulin into collagen in the later stages of the fibrotic process.

Curran (1952) showed that cortisone had no effect on existing silicotic lesions in the peritoneum of mice. Magarey and Gough (1952), working with rabbits, were unable to find any reduction of mature fibrous tissue in intraperitoneal silicotic nodules as a result of cortisone treatment, although histological evidence suggested that the administration of cortisone retarded the further proliferation of fibroblasts with consequent retardation of concentric fibrosis in the nodules, preformed collagen remaining unaltered.

It is concluded that cortisone has a modifying effect on developing silicotic fibrosis in the peritoneum and lungs of experimental animals, while its action on established silicotic fibrosis is less definite. It seemed desirable, therefore, to study the effect of cortisone on established silicotic fibrosis in the lungs of rats, with particular reference to the histological picture as well as to the collagen and silica content of the lungs.

Plan of Experiment

Thirty-six rats (M.R.C. black-and-white strain, ca. 250 g.) were given intratracheal injections of quartz dust (50 mg.) in order to produce silicotic fibrosis in their lungs. A sufficient period of time (100 days) was allowed for the formation of fully developed collagenous nodules, after which cortisone was administered to some of the animals. Three were lost by cannibalism, and the remaining 33 were divided into two groups; the first group of 11 animals served as controls and received no further treatment, while the 22 animals in the second group were given subcutaneous injections of cortisone acetate suspensions (5 mg. three times a week) over a period of 265 days. Animals from both groups were killed at regular intervals and histological examinations of the lungs carried out. Stacy and King (1954) have reported the collagen and silica contents of the lungs and lymph nodes estimated chemically.

Description of Samples

The dust used was powdered quartz "Snowit II". The sample was made by mixing two previously

TABLE 1

PARTICLE SIZE DISTRIBUTION AND ANALYSIS OF QUARTZ DUST USED FOR INTRATRACHEAL INJECTION

Size in μ	Percentage by No.	Percentage by Mass
0·32–0·45	3·0	—
0·46–0·64	18·9	1·5
0·65–0·9	38·2	7·9
1·0–1·3	16·8	9·6
1·4–1·8	12·3	20·2
1·9–2·6	9·5	43·7
2·7–3·6	1·3	17·1

Specific surface ($m^2/g.$)	1·8
SiO_2 (%)	98·7
Ignition loss (%)	0·17

prepared fractions from Belgian glass sand. Two-thirds by weight of a fraction of nominal diameter 1 to 2 μ. was mixed with one-third of a fraction 0·5 to 1 μ. in diameter. The resulting size distribution and the data obtained from chemical analyses are shown in Table 1.

The cortisone acetate suspension used in this work was a preparation from Merck & Co. Inc.

Preparation of the Dust Suspension

Quartz dust, 2·5 g., and sterile physiological saline 50 ml. were thoroughly shaken, autoclaved for 20 min. at 15 lb., and kept shaking in a microid flask-shaker till the time of injection. The final concentration of dust was 50 mg./ml. and this amount was injected into each animal.

Experimental Procedure

The animals were lightly anaesthetized with ether and the dust suspensions injected intratracheally via the mouth, according to the technique of Kettle and Hilton (1932), modified by King, Mohanty, Harrison, and Nagelschmidt (1953). There was no regurgitation of dust and no immediate post-operative deaths occurred.

Duration of Experiments

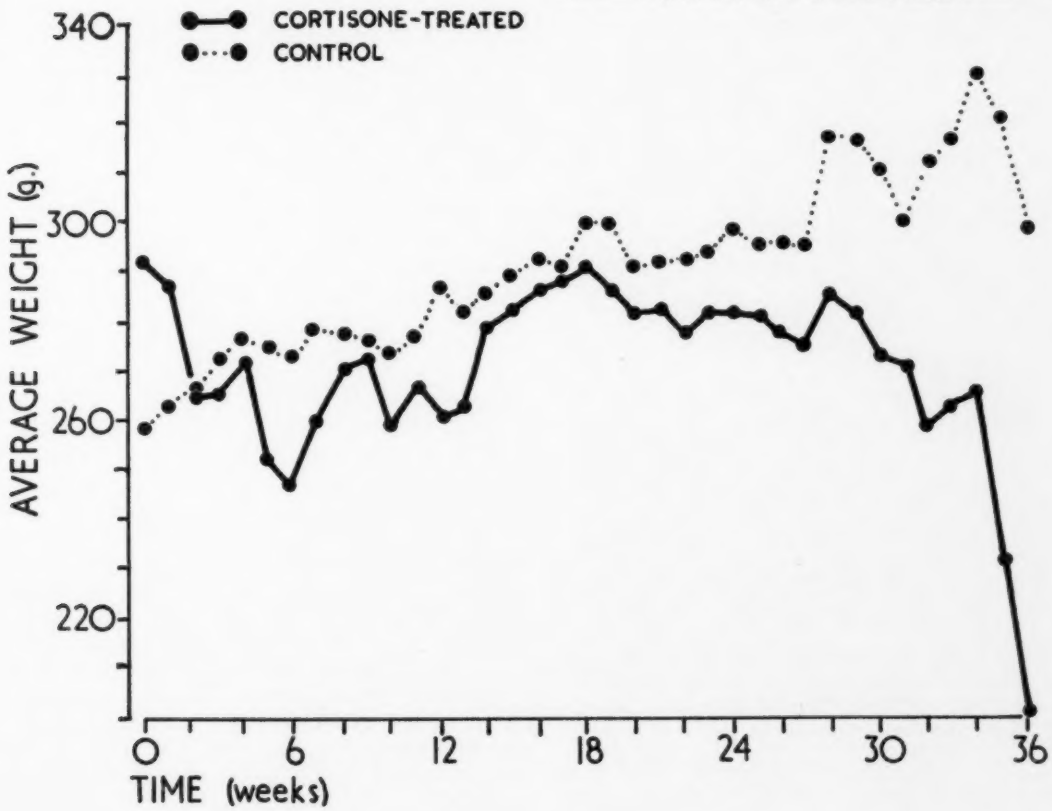
Cortisone injections were begun 100 days after the injection of quartz in the group of test animals. They were continued for 265 days (5 mg. three times a week). The animals were weighed at weekly intervals (Fig. 1).

A pair of animals, one from each group, were killed at fortnightly intervals in the early stages of the experiment. Owing to a number of deaths occurring in the group of cortisone-treated animals the intervals at which the killings were done had to be adjusted in order to extend the experiment over a sufficient period of time and to obtain equal days of survival in both groups. The experiment was concluded 365 days after the injection of quartz.

Histopathological Technique

Routine necropsies were carried out on the animals that were killed and on those found dead. Their lungs were removed and fixed in 10% formol-saline. The tracheo-bronchial lymph nodes were dissected out, weighed, and fixed separately. Blocks were taken along the long axes of both lungs through the hila, dehydrated, and embedded in paraffin wax. Serial sections, 5 μ in thickness, were stained by Gordon and Sweets' (1936) silver impregnation method for reticulin, and with

FIG. 1.—The effect of cortisone on the body weight of rats.



Ehrlich's haematoxylin and eosin. An unstained serial section was subjected to micro-incineration and then washed in concentrated HCl and dry-mounted.

Pathological Findings

Twenty-one days after the start of the cortisone injections the animals showed signs of moulting and bare patches appeared at the site of the injections. These patches became larger as the experiment progressed. During the first 42 days the animals lost weight steadily. The protein content in their diet was then increased and a slight improvement was noticed. Towards the end of the experiment they lost weight considerably, particularly during the last 56 days.

Amongst the 11 control animals there was one spontaneous death due to infection, while nine animals from the cortisone-treated group also died from infection. This is statistically significant and may be regarded as a result of cortisone treatment. The animals that died spontaneously, and whose lungs were found to be infected, were not used for histological comparison. Killings of animals from the two groups were adjusted as far as possible to obtain equal days of survival in both. The duration of the experiment, the days of survival of the animals, their mode of death, and the pathological grading of the lesions produced in their lungs, as assessed according to Belt and King (1945), have been summarized in Table 2.

TABLE 2
ASSESSMENT OF FIBROSIS IN LUNGS OF CORTISONE-TREATED AND CONTROL RATS PREVIOUSLY INJECTED WITH QUARTZ DUST

Days of Survival	Control		Cortisone-treated	
	Mode of Death	Grade of Fibrosis	Mode of Death	Grade of Fibrosis
122	D	—	—	—
123	K	4	K	4
124–150	K	5	K	5
			D (4)	—
			D	5
151–200	D	5	D	5
			D (4)	—
201–230	K	5	K	5
231–300	K *	5	K *	5
			D	5
			D	—
301–330	K	5	K (2)	5
331–365	K (4)	5	K (4)	5

* Sections from these animals are reproduced in Figs. 2 and 3.
K = Killed ; D = Dead ; Numbers in parentheses indicate the number of animals killed or found dead at the period.

Macroscopic Appearances of the Lungs.—On macroscopic examination there was very little difference between the lungs of the control animals and those which received cortisone.

Control Quartz Dust.—The lesions in the lungs were similar to those found previously in cases of quartz-induced fibrosis. At 123 days both lungs showed firm, white patches of fibrosis, which appeared to be running together in certain areas. By 150 days there were large areas of confluent fibrosis in the right lung, while in the left lung the fibrosis was mainly patchy. At 230 days the greater part of both lungs was replaced by confluent, white fibrous areas. From this period until the end of the experiment at 365 days, the naked-eye appearances of the lung were similar to those at 230 days, except that the amount of fibrosis in the lungs steadily increased. The lymph nodes were enlarged and firm from the first (123 days) and gradually enlarged further to several times normal as the experiment progressed.

Cortisone-treated Animals.—At 123 days there were firm, white areas of fibrosis in both lungs. They were mainly patchy, but showed a tendency to become confluent dorsally in some areas. The confluent areas had increased in size by 150 days and at 230 days most of the right lung showed areas of confluent fibrosis, while the left lung had a few discrete patches of fibrosis. After this the fibrosis seemed to increase as judged by the confluent areas seen macroscopically, and by 365 days most of the lung tissue was replaced by fibrous areas. The tracheo-bronchial lymph nodes were slightly enlarged and firm ; but, although they were larger than the lymph nodes of normal rats, were not as large as those found in the group of animals which had been injected with quartz dust without subsequent cortisone treatment.

Microscopic Appearances.—The pulmonary lesions in the animals which had quartz dust only and those which had subsequent cortisone treatment revealed no significant differences so far as the maturity of the fibrosis was concerned. But when paired lung sections from the two groups (animals killed at the same time) were examined with a hand lens there was a definite difference in the areas of lung tissue involved by the fibrous process. In the cortisone-treated animals, the area of lung involvement appeared to be less than in the controls.

Control Quartz.—The earliest sections examined were at 123 days, when the lungs showed numerous nodular foci typical of quartz fibrosis. The lesions were, for the most part, acellular at the centre, with some cellularity at the periphery. On reticulin staining they were seen to be composed entirely of compact collagen fibres (Grade 4 fibrosis). A few nodules showed a tendency to become confluent, but the majority were discrete. The fibrous process involved approximately one-third of the left lung field and one-half of the right one. By 150 days the lesions were confluent, acellular and collagenous

FIG. 2.—Control quartz rat lung 300 days after an injection of 50 mg. of quartz dust. Confluent silicotic nodule composed of compact collagen (Grade 5 fibrosis). Silver impregnation. × 36.

(Grade 5 fibrosis). About one-half of the areas of both lung fields was involved. At 230 days the histological picture was essentially the same as at 150 days, with about two-thirds of the left lung field and three-quarters of the right one replaced by confluent fibrotic lesions. From this period onwards the area of lung tissue involved increased, and at 300 days about three-quarters of both lung fields were replaced by confluent, acellular, fully collagenous lesions (Grade 5 fibrosis, Fig. 2). A few patent alveoli and some new-formed blood vessels were seen within the confluent areas.

Cortisone-treated Group.—The histological appearances of the lungs at 123 days were similar to those in the control animals. There were numerous nodular lesions throughout the lungs, involving about one-half the area of the right lung field and a little over one-third of the left lung. The lesions were discrete, mainly acellular, with cellularity only at the periphery, and on reticulin staining were completely collagenous (Grade 4 fibrosis). At 150 days many of the lesions were confluent, acellular, and fully collagenous (Grade 5), but the area of lung involved was about the same as at 123 days. The lesions at 230 days were no different from those at 150 days. By 300 days two-thirds of the area of the right lung field and one-third of the left were replaced by confluent, acellular, collagenous nodules (Grade 5 fibrosis, Fig. 3). An occasional discrete nodule was seen in some areas. Within the confluent fibrous lesions a few patent alveoli were seen. At 365 days the lesions were similar but the areas of lung involved were approximately one-half to two-thirds of one lung field and two-thirds to three-quarters of the other.

Discussion

In our experiments cortisone was administered to rats 100 days after intratracheal injection of quartz, when silicotic nodules were well developed. The histological lesions studied 123 days after the introduction of the dust—when one group of animals had had cortisone for 23 days—were very

FIG. 3.—Cortisone-treated quartz rat lung 300 days after the injection of 50 mg. of quartz followed by subcutaneous injections of cortisone (begun at 100 days and continued thrice weekly). Confluent collagenous lesions (Grade 5 fibrosis). Silver impregnation. × 36.

similar in both the control and cortisone-treated animals, there being fully collagenous nodules in both. At the end of the experiment, 265 days after the start of cortisone treatment, there was still no difference in the grade of fibrosis between the pulmonary lesions of the two groups, both being fully collagenous. Morphologically, the lesions in the control and cortisone-treated animals were identical; there were the same central collections of dust surrounded by dense collagen fibres. At the periphery of some lesions a few cells were seen, but this again was a common finding in the two groups.

Although there was no difference in the maturity of the fibrous tissue in the silicotic nodules of control rats and those treated with cortisone, there seemed to be a slight variation in the actual amount of lung tissue involved when paired sections from the two groups were compared. The cortisone-treated animals showed somewhat less involvement of lung tissue by the fibrous process, as compared with untreated animals, particularly in the later stages of the experiment. This was borne out by chemical estimations of collagen, which was found in smaller amounts in the lungs of cortisone-treated animals (Stacy and King, 1954).

These findings suggest that although cortisone has no effect on the quality of fibrous tissue it may affect the quantity formed. Presumably, the silicotic nodules which were present in the lungs at the time the cortisone treatment was begun were generally prevented from enlarging without any actual resolution of the fibrous tissue taking place.

This aspect of our present finding is in keeping with the results of Marenghi and Rota (1954) who also found a great difference in the total degree of pulmonary fibrosis between their cortisone-treated and control animals, though in their experiment the difference was more striking than in ours.

From these results it is evident that cortisone has no beneficial effects on pulmonary silicosis in animals when administered after the formation of mature silicotic nodules. Harrison and others (1952) were unable to prevent the development of quartz-induced pulmonary fibrosis in rats by the administration of cortisone, even though the treatment was begun almost with the introduction of the fibrogenic agent and pushed to the limit of tolerance.

Although it is not justifiable to apply these findings to man, nevertheless, it seems unlikely that cortisone would have any beneficial effect on human silicosis.

Summary

The effect of cortisone on established silicotic fibrosis in the lungs of rats was studied by the intratracheal injection of 50 mg. of quartz dust in rats, followed 100 days later by the administration of 3 mg. cortisone acetate three times a week for 265 days.

Cortisone did not alter the pattern of the fibrosis or bring about any regression of existing silicotic nodules. Mature collagenous lesions were present in the control and cortisone-treated animals at all stages of the experiment. The actual amount of lung tissue involved by the fibrotic process was slightly less in the cortisone-treated animals when paired histological preparations from the two groups were compared.

It is concluded that cortisone does not have any appreciable effect on established silicosis as far as the grade of fibrosis is concerned, although a slight reduction in the actual amount of fibrous tissue may be found.

Cortisone retards the phagocytic transport of dust from the lungs to the lymph nodes. There was more silica remaining in the lungs of the cortisone-treated animals than in the controls, while their lymph nodes contained less than the control nodes (Stacy and King, 1954).

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LEPTOSPIROSIS IN SOUTH-EAST SCOTLAND

A REPORT OF TWENTY SEROLOGICALLY CONFIRMED CASES

BY

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In the period 1947–50, 465 cases of Weil's disease were reported in England, Wales, and Northern Ireland, and 70 human cases of *Leptospira canicola* fever in England and Wales (Broom, 1951). An analysis of 418 of the cases of Weil's disease showed that 31% occurred in farm workers. Bathing and accidental immersion accounted for 19%, and 31% were in persons of "miscellaneous" occupations. Sewer workers, coal-miners, food-handlers, fish workers, and workers in water made up the remaining 19%. The mortality rate was 15%, which compares with the rate of 22% recorded for the period 1940–46 by Broom and Alston (1948).

In Scotland, reports of leptospirosis have on the whole been connected with definite occupations. Thus Weil's disease was reported in coal-miners by Gulland and Buchanan (1924), by Jenkins and Sharp (1946), and by Sharp (1953). The total number of cases among coal-miners notified from 1924 to 1951 and reported by the latter two workers was 101, of which 29 died. The districts mainly concerned were East Lothian, Midlothian, Fife, and the Clyde Valley, this last supplying more than half the total cases.

Smith (1949) has reviewed the incidence of Weil's disease in north-east Scotland, including Orkney and Shetland, from 1934 to 1948 and in his series described 183 cases occurring in fish workers in Aberdeen (including 98 reported by Davidson and Smith in 1939).

In the Glasgow fishmarket, six sporadic cases of Weil's disease, occurring during the period 1944–50, were reported by Goudie, Weir, and Wilson (1952), together with a description of working conditions and their relation to leptospiral infection.

Sewer workers have provided relatively more published cases of leptospirosis in Scotland than in England. Thus, following Stuart's investigation (1938) into Weil's disease in Glasgow sewermen, Bell (1953) reported that a total to date of 28 cases had occurred among these workers, 23 of them since 1935.

Though Broom showed that farm workers supply the bulk of cases in England and Wales, no published record seems to be available so far of Weil's disease in Scottish farm workers. Meat-handlers represented 19·5% of 46 cases reported to the Glasgow Health and Welfare Department between 1926 and 1949, bathing and accidental immersion were responsible for 13%, and 15·4% represented other occupations. Coal-miners, sewer workers, and fish workers together accounted for 50% of the Glasgow figures (Bell, 1953).

The incidence of leptospirosis in rats in Scotland has been estimated at 44% of 117 rats in the Aberdeen district by Smith in 1938 (56% of fully grown animals), while 37% of 166 rats in East Lothian were found to be infected (Buchanan, 1927).

Although Weil's disease has been notifiable in Scotland since 1924, *Leptospirosis canicola* is not, and records of previous human cases are limited to three described by Joe and Sangster (1951) and three mentioned by McIntyre and Seiler (1953), two of which (patients B and C) are also included in the present series.

Leptospiral infection of dogs on the other hand is very widespread, and surveys, *e.g.*, by Stuart (1946) and Broom and MacIntyre (1948), have shown evidence of infection with *L. canicola* in 21 to 40% of dogs. The very low human infectivity of this organism at present in Scotland, however, is shown by the negative results of serological tests, which I carried out and which were reported by McIntyre and Seiler (1953), on the sera of 99 household contacts of dogs known to have had *L. canicola* infection at the time of contact.

The present report details 19 serologically confirmed cases of leptospirosis due both to *L. icterohaemorrhagiae* and *L. canicola*, which have occurred during the period October, 1950, to December, 1953, in south-east Scotland and one case in Falkirk. For the purposes of this report south-east Scotland is taken as comprising Edinburgh, the Lothians, Peebles, Roxburgh, Selkirk, and Berwick.

Methods

The serological data presented in this paper were obtained from the routine examination of sera carried out in the laboratories of the University of Edinburgh and the Royal Infirmary, Edinburgh. Information regarding epidemiology and clinical features was obtained from the clinicians concerned, and is published with their permission.

Blood specimens were received from hospitals and general practitioners and the sera were examined for the presence of agglutinins for leptospirae. Living cultures were used and a dropping technique similar to that of Schüffner and Mochtar (1927) was adopted. Results were read after two hours at 37° C. and a further two hours at room temperature by dark-ground microscopy. Strains of leptospirae used included *L. icterohaemorrhagiae* (Wijnberg), *L. canicola* (Berlin), and *L. canicola* (Utrecht IV).

Where possible, repeated samples of serum were examined until the titre against one or other of the two types was (a) at least 1 in 1,000 and (b) at least 10 times greater with one type than with the other. This ten-fold difference (usually it was even more) was taken as sufficient evidence, when occurring in the later stages of the disease, to indicate the causative type without the need for absorption tests.

Five rats which had been trapped alive on one farm were killed by coal gas and examined for leptospiral infection by injecting the emulsified kidneys into young white guinea-pigs. Cultures in Korthov's medium (modified as described in Mackie and McCartney's handbook, 1953) were made from the guinea-pig tissues when jaundice appeared, and their identity confirmed by agglutination to titre by stock antiserum.

Results

The occupational incidence of the series is shown in Table 1. It will be seen that the bulk of the cases occurred in the occupations of coal-miner and agricultural worker for both Weil's disease and *L. canicola* fever. The probability of contact with rats was established in 12 of the 14 cases of Weil's disease and with dogs in three of five cases of *L. canicola* fever.

TABLE 1

INCIDENCE OF WEIL'S DISEASE AND *L. CANICOLA* FEVER ACCORDING TO OCCUPATION

Occupation	Number of Cases		
	Weil's Disease	*L. Canicola* Fever	Total
Coal-miner	5	2	7
Agricultural worker	4	2	6
Gamekeeper	1	—	1
Steelworker	1	—	1
Blacksmith	1	—	1
Motor-driver	1	—	1
Schoolboy	1	—	1
Street orderly	—	1	1
Gasworks maintenance worker	—	1	1
Totals	14	6	20

The incidence of Weil's disease and *L. canicola* fever according to locality is seen in Table 2.

TABLE 2

INCIDENCE OF LEPTOSPIROSIS ACCORDING TO LOCALITY

County	Town	Weil's Disease	*L. Canicola* Fever
Midlothian	City of Edinburgh	3	4
	Currie	—	1
	Loanhead	—	1
	Newtongrange	2*	—
	Gorebridge	2	—
East Lothian	Pencaitland	1	—
	Prestonpans	1	—
Roxburgh	Kelso	2	—
	St. Boswells	1	—
Berwick	Earlston	1	—
Stirling	Falkirk	1	—

*One of these two miners lived at Prestonpans in East Lothian, but worked in a Newtongrange pit known to be damp and rat-infested.

Although Earlston is in a different county from Kelso and St. Boswells, all these three towns are within 10 miles of each other. An examination of five rats trapped on the farm where one of the Gorebridge patients worked showed that four of the rats harboured *L. icterohaemorrhagiae* in the kidneys.

Incidence according to age, sex, and season was as follows. Cases of Weil's disease were fairly evenly distributed over the decades from 10 to 70. Those of *L. canicola* fever were limited to the age group 10 to 40. Of the three fatal cases of Weil's disease, all occurred in men over 40 and two of these were over 50. All the cases, both of Weil's disease and *L. canicola* fever, occurred in males, while 14 of the total of 20 occurred in the second half of the year (July to December inclusive). One case occurred in October, 1950, six in 1951, five in 1952, and eight in 1953.

The predominant clinical features, as shown in Table 3, included fever, headache (usually severe), vomiting, and jaundice. A raised erythrocyte sedimentation rate was present in all of the 15 cases in which it was ascertained. Urinary symptoms or signs, *e.g.*, dysuria, increased frequency of micturition, albuminuria, pyuria, and red cells and casts in the urine, were present in eight out of 13 cases of Weil's disease and in two of the six of *L. canicola*. A haemorrhagic tendency was manifested in seven out of 13 cases of Weil's disease, but in none of *L. canicola* fever, by haemoptysis, haematemesis, melaena, epistaxis, bleeding into lip herpes, or generalized petechiae. Cerebrospinal fluid was taken in a total of seven instances out of the 10 in which meningeal signs were present, and these specimens showed a raised cellular content, mainly polymorphic

TABLE 3

PREDOMINANT CLINICAL FEATURES

		Number of Cases		Total
		Weil's Disease	*L. Canicola* Fever	
Fever (usually with rigor and varying between 100 and 104° F.)		11	5	16
Headache	Severe	8 (12)*	6	18 (18)
	Moderate	4 (12)	—	
Vomiting		11	4	15
Muscular pains		7	3	10
Injection of conjunctivae		6	2	8
Raised E.S.R. (12 mm. or more in the first hour)		11 (11)	4 (4)	15 (15)
Urinary symptoms or signs		8 (13)	2	10 (19)
Raised blood urea nitrogen (40 mg. % or more)		6 (8)	Not done	—
Jaundice		11	1	12
Haemorrhagic manifestations		7 (13)	0	7 (19)
Meningeal signs		5	5	10
Cerebrospinal fluid :				
Increased cells		3 (3)	4 (4)	7 (7)
Protein		2 (3)	4 (4)	6 (6)
Sugar over 50 mg. %		3 (3)	3 (4)	6 (7)

* The figures in parentheses refer to the number of cases in which observations were made, where this is less than the total number of patients involved.

(lymphocytic in one *L. canicola* case), and with raised protein. The sugar content was over 50 mg.%, with the exception of one specimen where it was 45 mg.%.

Blood serum agglutinin titres were of the usual high level associated with leptospiral infection. Apart from one rapidly fatal case, the maximum titre attained in any one case was always 1 in 1,000 or more, and in seven cases a titre of 1 in 30,000 or over was reached, four of these being cases of *L. canicola* fever, one of which gave a titre of 1 in 100,000 on two occasions. The rule already mentioned of requiring at least a ten-fold difference between homologous and heterologous titres occurring in the later stages of the illness was adhered to with the exceptions shown in Table 4.

TABLE 4

SEROLOGY OF CASES 5, 10, AND 18

Case	Days after Onset	Serum Titre* against	
		L. icterohaemorrhagiae	*L. canicola*
5	9	5,000	50
	18	10,000	Not done
	5 months	1,000	Not done
10	5	1,500	1,000
18	?	64	64

* Titres expressed as the reciprocal of the final dilution at the end-point.

In Case 5, the 100-fold titre difference against the two leptospira species on the ninth day of illness, together with the prolonged duration of the high titre against *L. icterohaemorrhagiae*, made the diagnosis of Weil's disease certain. Cases 10 and 18 died immediately after admission to hospital, in cholaemia. In these, jaundice and typical post-mortem findings, together with the history of contact with rats, completed the picture of Weil's disease.

Discussion

The fatality rates of three out of 14 cases of Weil's disease and three out of a total of 20 of leptospirosis (including those due to *L. canicola*) compare with Broom's (1951) mortality rate of 15% for England and Wales in 1947–50, the rate of 22% given by Broom and Alston for the period 1940–46, and the figure of 29% obtained from data concerning Scottish coal-miners published by Jenkins and Sharp (1946) and Sharp (1953).

Penicillin was given in 13 cases, but in only one was there any obvious effect, that of Case 8, where the patient was said to have " responded well " to 200,000 units thrice daily to a total of 4·2 mega units, with a marked fall of temperature during the first day of treatment. Since the penicillin was not given until quite late in the disease, it seems unlikely that the effect was due to the anti-leptospiral action of the drug. In the one fatal case which was given penicillin, treatment was not started until a week after the onset of the illness, and could not therefore be expected to affect the issue.

That there is a symptomatology common to the leptospiroses as a whole, with only relatively minor variations in kind between infections due to different serological varieties, is illustrated by the similar incidence of certain symptoms in Weil's disease and *L. canicola* fever in the present series. Thus fever of over 100° F., usually with rigor at the onset, moderate to severe headache, vomiting, a raised E.S.R., muscular pains, and injection of the conjunctivae occurred with nearly equal frequency in the two forms of leptospirosis concerned. Clinical differences included markedly greater frequency of jaundice and haemorrhagic manifestations in Weil's disease, and of meningeal signs in *L. canicola* fever. Urinary signs were recorded more often in Weil's disease. The high incidence of haemorrhages in Weil's disease is in accord with the higher fatality rate, but it should be noted that of the seven instances of haemorrhage, four occurred in patients who made a good recovery. The finding of a constantly raised E.S.R. is in accord with the results of Litzner and Hahn (1950), who were even

prepared to rule out the possibility of making a diagnosis of leptospirosis in the presence of a normal sedimentation rate.

Cerebrospinal fluid findings were in keeping with the generalized nature of leptospiral infection, but the relatively normal levels of sugar were in agreement with the observations of, for example, Glattkowski (1950), that concentrations of 50 mg. % or more are the rule in leptospirosis as against the lower levels found in tuberculous meningitis (Rubie and Mohun, 1949).

Summary

Nineteen serologically confirmed cases of leptospirosis occurred in south-east Scotland (excluding Fife) and one in Falkirk in the period October, 1950, to December, 1953, including 14 cases of Weil's disease and six of *L. canicola* fever.

Details are given of incidence according to occupation, age, sex, locality, and season, and the predominant clinical features are discussed.

Leptospira icterohaemorrhagiae were isolated from four out of five rats rats trapped in one of the localities concerned.

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THE ENERGY COST OF SOME INDUSTRIAL OPERATIONS

BY

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This study forms part of a larger investigation carried out in 1947-48. It aimed at providing a hospital department of cardiology with information regarding the physical effort involved in doing various standard operations. This information was for the use of physicians in advising patients and disablement resettlement officers regarding suitable work. Although the investigation was by no means extensive and the numbers of observations were small, the results appear to be of some value, especially in view of the present interest in the employment of elderly persons.

Method

Two methods were used for assessing the arduousness of each process. The first was the determination of the metabolic rate of the workers, and the second a subjective assessment, based on a simple "job-analysis". The subjective assessment was always made before any measurement of the metabolic rate.

Metabolic Determinations.—Several workers on each process were examined. Their metabolic rates were determined during a typical period of the working day by the Douglas-Haldane technique. In preference to the normal type of mouthpiece, a rubber face mask, strapped to a webbing harness worn on the head, was used for collecting the expired air. This had the advantage of preventing any leakage of air by the worker failing to maintain a firm grip on the mouthpiece, and of minimizing the distraction from normal working procedure due to the wearing of respiratory apparatus. The air expired during a known time was collected in a Douglas bag worn on the back, and samples were analysed in the factory by means of a standard Haldane gas analysis apparatus.

The face piece was made by Siebe, Gorman and Co. It was basically of rubber-covered copper, malleable to fit any size or shape of face, with an air cushion round the outer rim to provide an airtight shield. Both inlet and outlet valves were incorporated. The period of acclimatization was at least 10 minutes, and always until breathing was at a normal rate. The apparatus was worn for a further five minutes, or until the Douglas bag was full.

For classification of processes on a metabolic basis, a scale which had been used by Orr and Leitch (1937) was adapted. In its original form that scale classified processes according to the excess metabolism per hour over the resting level in an "average" man of surface area 1·77 sq. m. Converted into terms of total metabolism at work per sq. m. of body surface per hour, the scale becomes :

Light work : Up to 90 calories per sq. m. per hr.
Moderate work : 90–134 calories per sq. m. per hr.
Heavy work : 135–220 calories per sq. m. per hr.
Very heavy work : Over 220 calories per sq. m. per hr.

This was the scale used in the present investigation.

Subjective Assessments.—The investigator made a rough analysis of each process, noting such factors as the time taken for a complete cycle of the operation, the apparent severity of the physical effort involved in the various phases of the work-cycle, the amount of walking and lifting necessary, and any other particular sudden stresses. After this analysis the overall severity of the process was assessed and denoted by placing the operation in one of three classes, A, B, or C. Class A contained those jobs which seemed to involve heavy or very heavy work, class B those of moderate severity, while class C consisted of the light jobs. Each process was then placed in one of three groups within its class. Group 1 denoted that there was considerable variation in the apparent rate of energy expenditure at various times in the cycle, group 3 denoted a relatively steady rate during the whole working time, and group 2 was intermediate.

The analysis notes which were made at the time of observation are not reproduced here. They were rough by comparison with modern time-study methods, and were meant merely as a brief description of a process for the benefit of persons unfamiliar with it. The following is an example, namely the analysis of plate casting.

The operator stands at a mould beside a vat of molten lead. Some moulds are gas-heated. A small scoopful of lead is poured into the mould, then a small quantity of cold water, and the mould is opened. The plate is removed and put aside, the

mould surfaces sprayed, the mould closed and refilled. The cast plates are stacked away when cool. One cycle of operations takes about half a minute. Working conditions are very warm. Sustained effort is required.

Results

The investigation was made in three factories (plastics moulding, electric accumulator manufacture, and engineering) and in two Government training centres.

In all, 287 metabolic determinations were made, including 59 on women, and 48 different processes were examined. The results of the experiments are given in Tables 1 to 3, where the metabolic cost and classification are compared with the subjective assessment into a sub-division of class A, B, or C.

Only on rare occasions was more than a single determination of metabolic rate made on one individual. The majority of the observations made on women may be found among the results in Table 3. Ebonite and plastic finishing, fixing rubber to plates, typing, comptometer operating, and card punching account for most of them. It is difficult to say more than that women were found in the light jobs, since in most cases both men and women were doing the job.

It will be seen from Tables 2 and 3 that there was close agreement between the two systems in the medium and light ranges of work. Of 16 processes arbitrarily assessed as class B, 15 were of medium severity according to the metabolic scale of Orr and Leitch. The remaining occupation (typewriter mechanic trainee) would have been classified as light work according to the average of the metabolic tests, but of the six tests made on this task the result of one fell within the range of medium work. Table 3 shows that in all the operations classed as "light work" there was complete agreement between the arbitrary judgments and the metabolic classification. With the heavier processes (Table 1) the agreement is not so close, for there was a tendency for the observer to overestimate the severity of this work. The arbitrary judgments were consistent amongst themselves, however, and a correction for this tendency could be applied if necessary.

The frequency distributions show that the individual readings for some processes vary widely. Such variation usually indicates that the operation is not of a routine nature but varies in character from time to time, as, for instance, in a skilled trade such as machine fitting or joinery. This variation may be partly responsible for the discrepancies between the two classifications, as the observer would probably tend to bias his classification in favour of the more strenuous phases of the work. Indeed, when such a classification of operations for use in the placement of unfit persons is made on the basis of metabolic measurements, it would be well to rank operations which show much variation as somewhat more severe than the mean metabolic rate indicates, thus allowing for temporary stress.

TABLE 1

METABOLIC COST OF OPERATIONS RATED AS HEAVY OR VERY HEAVY IN SUBJECTIVE APPRAISAL

Operation	Arbitrary Classification	Metabolic Classification	Working Metabolism (Calories per Square Metre per Hour)												Total No. of Observations	Mean Metabolic Rate
			90–99	100–109	110–119	120–129	130–139	140–149	*150–169	170–189	190–209	210–229	230–249	250–269	270–289	
Unloading battery boxes from oven	A1	Very heavy	—	—	—	—	—	—	—	—	—	2	2	—	—	4	230
Loading chemicals into mixer	A1	Heavy	—	—	—	—	—	—	—	1	—	1	—	—	—	2	200
Heavy millroom work (ebonite moulding)	A3	Heavy	—	—	—	—	—	—	—	1	1	—	—	—	—	2	190
Machine-moulding battery plates	A3	Heavy	—	—	—	—	—	—	1	1	—	—	—	—	—	2	170
Heavy assembly line work	A3	Heavy	—	—	—	—	1	1	—	1	1	—	—	—	—	4	160
Casting lead balls in mould	A2	Heavy	—	—	—	—	—	—	2	—	—	—	—	—	—	2	160
Straightening lead contact bars	A3	Heavy	—	—	—	—	1	—	1	1	—	—	—	—	—	3	155
Machine sawing	A3	Heavy	—	—	1	1	1	—	—	1	1	—	—	—	—	5	145
Trimming battery plates	A2	Heavy	—	—	—	1	—	1	—	1	—	—	—	—	—	3	150
Loading battery plates into oven	A2	Heavy	—	—	—	—	1	—	1	—	—	—	—	—	—	2	145
Heavy battery case fabrication	A3	Heavy	—	1	—	—	1	1	2	—	—	—	—	—	—	5	140
Heavy battery plate casting	A3	Heavy	—	—	—	1	—	3	—	—	—	—	—	—	—	4	140
Machine fitting	A1	Heavy	4	—	—	2	1	1	2	—	—	1	—	—	1	12	140
Lead rolling on roller mill	A3	Moderate	—	1	—	—	—	2	—	—	—	—	—	—	—	3	130
Hand and machine plate pasting	A3	Moderate	1	—	1	1	3	1	1	—	—	—	—	—	—	8	130
Loading plates into charging vat	A3	Moderate	—	—	3	2	1	—	2	—	—	—	—	—	—	8	130
Moulding ebonite	A2	Moderate	1	2	—	1	1	2	—	—	—	—	—	—	—	7	120
Light battery plate casting	A2	Moderate	—	2	1	—	3	—	—	—	—	—	—	—	—	6	120

* Change of class interval.

TABLE 2

METABOLIC COST OF OPERATIONS RATED AS OF MODERATE SEVERITY IN SUBJECTIVE APPRAISAL

Operation	Arbitrary Classification	Metabolic Classification	Working Metabolism (Calories per Square Metre per Hour)														Total No. of Observations	Mean Metabolic Rate
			50–59	60–69	70–79	80–89	90–99	100–109	110–119	120–129	130–139	140–149	*150–169	170–189	190–209	210–229	230–249	
Tool-room workers	B2	Moderate	—	—	—	—	—	1	1	1	—	—	—	1	—	—	—	4	130
Turners	B2	Moderate	—	—	—	—	—	1	1	—	2	—	—	—	—	—	—	4	125
Joiners	B3	Moderate	—	—	1	3	2	3	3	2	—	1	1	1	—	—	1	18	120
Light battery case fabrication	B3	Moderate	—	—	—	—	—	3	1	—	1	—	—	—	—	—	—	5	115
Cutting battery plates	B3	Moderate	—	—	—	1	3	3	3	2	1	—	1	—	—	—	—	14	110
Plastic moulding	B2	Moderate	—	—	—	2	2	1	1	—	1	2	—	—	—	—	—	9	110
Punching battery plates to size	B2	Moderate	—	—	—	—	2	—	2	—	1	—	—	—	—	—	—	5	110
Light millroom (ebonite)	B2	Moderate	—	—	—	2	1	—	1	—	1	—	—	—	—	—	—	5	105
Machinists (engineering)	B2	Moderate	—	—	2	2	1	3	1	—	2	1	—	—	—	—	—	12	105
Sheet metal worker	B2	Moderate	1	—	—	1	2	1	2	—	—	1	—	—	—	—	—	8	100
Joiner (trainee)	B2	Moderate	—	—	—	—	4	3	—	1	—	—	—	—	—	—	—	8	100
Connecting battery plates for charging	B2	Moderate	—	—	—	1	1	—	1	—	—	—	—	—	—	—	—	3	100
Boot and shoe repairer (trainee)	B2	Moderate	—	—	1	1	—	2	1	—	—	—	—	—	—	—	—	5	95
Welding	B1	Moderate	—	—	—	—	1	1	—	—	—	—	—	—	—	—	—	2	95
Medium assembly work	B3	Moderate	—	1	4	2	2	1	2	2	—	—	—	—	—	—	—	14	90
Typewriter mechanic (trainee)	B3	Light	—	5	—	—	—	1	—	—	—	—	—	—	—	—	—	6	70

* Change of class interval.

TABLE 3

METABOLIC COST OF OPERATIONS RATED AS LIGHT IN SUBJECTIVE APPRAISAL

Operation	Arbitrary Classification	Metabolic Classification	Working Metabolism (Calories per Square Metre per Hour)								Total No. of Observations	Mean Metabolic Rate
			40–49	50–59	60–69	70–79	80–89	90–99	100–109	110–119		
Ebonite and plastic finishing	C3	Light	—	2	2	6	3	2	1	2	18	80
Light machine work (engineering)	C2	Light	—	1	—	4	1	2	—	—	8	80
Fixing rubber insulation to battery plates	C3	Light	—	—	1	1	1	—	—	—	3	75
Typing	C3	Light	—	1	2	2	—	—	—	—	5	70
Draughtsman	C3	Light	—	2	1	2	—	—	—	—	5	60
Comptometer operating	C3	Light	—	2	2	—	—	—	—	—	4	60
Drilling (training centre)	C3	Light	—	2	—	1	—	—	—	—	3	60
Light assembly line	C3	Light	—	1	2	—	—	—	—	—	3	60
Inspecting wooden separators	C3	Light	—	3	1	—	—	—	—	—	4	60
Tailor (trainee)	C3	Light	1	6	2	—	—	—	—	—	9	55
Card punching for mechanical accounts	C2	Light	3	2	1	—	—	—	—	—	6	50
Watch and clock repairer (trainee)	C3	Light	3	4	1	—	—	—	—	—	8	55

The chief function of the arbitrary grouping, in conjunction with an overall assessment of effort, is to indicate whether a process demands the use of energy at a steady rate or whether the work is done in bursts interspersed with rest pauses. There does not appear to be any simple method of checking the accuracy of this grouping.

The results of this investigation indicate that an observer can classify occupations with a fair degree of accuracy after a little experience without making any physical measurements. Thus a single observer could rapidly survey the processes in local industry and compile an index of classifications and analytical notes of sufficient accuracy to be of help to medical officers when they are suggesting suitable employment for the unfit.

Summary

Assessments of the severity of the work involved in 48 industrial processes are reported. The assessments were made on two bases : (1) measurements of the metabolic rate during work, and (2) subjective appraisal by an observer. Close agreement between the two methods of assessment suggests that for the placement of unfit or elderly workers satisfactory results can be obtained without recourse to metabolic measurements. A single observer could rapidly survey processes in local industry and compile an index of suitable occupations which should be of value to medical officers.

I wish to express my indebtedness to Professor R. E. Lane for the facilities to carry out this study and for his unfailing interest and encouragement, to Professor W. Schlapp for much guidance, and the loan of the necessary physiological apparatus, and to the many persons in industry without whose willing cooperation the results could not have been obtained.

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CUTTING OILS AND SQUAMOUS-CELL CARCINOMA

PART I: INCIDENCE IN A PLANT WITH A REPORT OF SIX CASES

BY

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(RECEIVED FOR PUBLICATION JANUARY 25, 1955)

The occurrence of skin cancer in machine operators is of interest because of its possible relation to exposure to petroleum products, chiefly the cutting oils. When, therefore, six cases of squamous-cell carcinoma of the skin have become known at a single machine-operating plant the cases are considered of sufficient importance to warrant reporting with some observations on both clinical histories and incidence rates during the last 10 years.

The plant concerned has been in operation since before 1920. Both manual and automatic machines of different types have been used. A medical centre is maintained in the plant with a part-time physician.

It is not known if the cases reported represent all those which occurred during this period. Records are not available covering the retired, transferred, or terminated workers. There is also a possibility that cases existed for which there are no available records.

Details of these six cases (Cases 1 to 6) and of one case of skin papilloma (Case 7) are given below.

Case Reports

Case 1.—This man, born in 1896, started at the plant in 1920 as the operator of a horizontal broacher which splashed oil towards the lower abdomen of standing operators. It had been his main employment. In January, 1950, he noticed a slight chafing on the right side of the scrotum which subsequently became infected. This condition, however, was not reported to the plant physician until nearly 12 months after the initial symptom. By this time there was an indurated ulcer about 1½ in. in diameter on the right side of the scrotum with some enlargement of the lymph glands in the right groin. He was admitted to hospital and the lesion was widely excised in January, 1951. The histological diagnosis was squamous-cell carcinoma, grade III. The lymph glands in the inguinal and femoral regions were bilaterally dissected at a second operation and biopsy of these glands showed no evidence of metastatic growth. This man is still at work as a supervisor.

Case 2.—A man, born 1896, was first employed at the plant in 1935 and had operated various machines. In September, 1950, he suffered a minor laceration on the back of the right hand. A swelling, thought to be caused by an embedded steel fragment, developed at this site. It was excised about a month after the original injury. Routine biopsy examination revealed squamous-cell carcinoma, grade I. This man is still at work at the plant.

Case 3.—For 22 years this man, born in 1900, had worked as a gear cutter in another plant with similar working conditions. In 1932, while employed at this plant, he had dermatitis of both forearms. Since this time he has suffered from dermatitis of both forearms intermittently. In 1947 he transferred to the present plant. For a short time he operated automatics and later various other machines. In September, 1950, several infected papules appeared on the right forearm. One did not respond to treatment but remained as a swelling. The plant physician referred him to a dermatologist for consultation; the clinical diagnosis was epithelioma. The lesion was excised in November, 1950, and the histological diagnosis was squamous-cell carcinoma, grade I. In June, 1953, he was admitted to hospital because of traumatic pneumonitis following an injury to the chest wall. During this admission several growths of the lower abdomen and thighs were noted. One of these, a growth on the right side of the abdomen, was removed and when examined microscopically was found to be squamous-cell carcinoma, grade I. This man is still at work.

Case 4.—This man, born in 1905, began work in 1929 on the automatic machines. He had been, however, mainly occupied in other machine work. In November, 1942, he noticed a swelling on the right forearm which gradually increased in size. This was excised and microscopic examination revealed epidermoid carcinoma (low grade). In 1944 he began to suffer from recurrent dermatitis of both forearms. A dermatologist reported his condition in June, 1944, as follicular keratosis with a developing ulceration of the left forearm, clinically malignant. Radium treatment controlled this lesion satisfactorily but in follow-up visits some enlargement of

the lymph glands in the left axilla was observed. A radiologist advised excision of these glands. This was done in November, 1944. No secondary growth was observed in the dissected lymph glands. Upon recovery he returned to his former work. In 1952 a further lesion occurred on the right forearm. This was excised in December, 1952, and diagnosed as squamous-cell carcinoma, grade I. He is still at work at the plant.

Case 5.—In 1924, this worker, a man born in 1894, began as an operator on the automatic machines, later becoming a set-up man, and eventually a supervisor. In May, 1953, he reported to the medical centre with dermatitis involving both wrists and forearms. Shortly afterwards a warty growth appeared on the right wrist. This was excised in August, 1953. Microscopic examination revealed it as squamous-cell carcinoma, grade I. A second lesion occurred and was removed from the left forearm in November, 1953, with a similar histological diagnosis. He is still at work.

Case 6.—This workman, born in 1902, started at the plant in 1935 as an automatic machine operator. He suffered from an oil dermatitis in 1944 but it cleared without trouble. In July, 1952, he was seen with multiple keratoses of both forearms. These were considered clinically as precancerous lesions and removal was recommended. Several were excised in July, 1952, and were described histologically as presenting the picture of senile keratosis. Since the first excision many keratotic lesions have been removed by excision, dessication, curettage, or *x*-ray treatment. In October, 1952, a lesion removed from the left forearm showed evidence of low-grade malignancy (squamous-cell carcinoma, grade I). Numerous lesions removed subsequently from both forearms were described microscopically as oil keratosis. This man died suddenly at work in November, 1954, of heart disease.

Case 7.—This man, born in 1891, gave a history of almost unbroken employment as a machine operator since 1907. In 1925 he started to work at this plant as a set-up man on automatic machines. In May, 1945, he was seen by the plant doctor with an infected oil dermatitis of both forearms. In July of that year a consultant noted many hyperkeratotic lesions on both forearms and on the scrotum. There was a cutaneous horn on the dorsum of the right hand. At that time some of the lesions were described as potentially malignant. In October, 1945, four such lesions were excised, two from the right forearm, one from the left forearm, and one from the scrotum. Microscopic examination revealed no definite malignant change. One lesion from the right forearm was described microscopically as a papilloma and the lesion from the scrotum was described as having papillae which dipped very deeply into the corium. This workman returned to the plant after removal of the lesions. He was then given work away from oil. Despite this, hyperkeratotic lesions continued to develop and he left the plant in 1947 with the clinical diagnosis of chronic occupational dermatitis. He has been seen regularly since 1947 with a persistent dermatitis and numerous hyperkeratoses over both forearms and hands.

Observations on the Case Histories

From the data presented in Table I it can be seen that the age at onset of carcinoma ranges from 37 to 59 years with an average of 51.

The length of employment in the plant varied from three to 31 years. The workman who had worked only three years should rightly be excluded, since he had been similarly exposed before. When this is done the years of exposure of the remaining five cases varies from 13 to 31 years with an average period of 21 years.

TABLE I
SUMMARY OF DATA ON PLANT CASES

Case	Machines Operated	Age at First Lesion	Plant Exposure (Years)	Original Site	Subsequent Carcinomata
1	Broacher	55	31	Scrotum	
2	Various	54	15	Right hand	
3	Various	50	3*	Right forearm	Abdominal wall (1953)
4	Various and automatics	37	13	Right forearm	Left forearm (1944) Right forearm (1952)
5	Automatics	59	29	Right wrist	Left forearm (1953)
6	Automatics	50	17	Left forearm	
7	Automatics	54	20	Right forearm	

* This man worked 22 years at similar work in previous employment.

The site of the first lesion in these cases is interesting. The exposed skin of the hand and forearm is involved in all cases except one which is of the scrotum. It is interesting also to observe that the right side is involved as the site of the first lesion in five of the six upper limb cases.

Three of the cases of carcinoma and the one case of papilloma did most or all of their work on automatic machines. Automatic machine workers comprise only about 5% of male machine operators.

The Incidence Rate

It is important to realize that in this study of the incidence of skin carcinoma the derived rates are based on only six reported cases. Furthermore, it was decided arbitrarily to study the reported cases in relation to the male population of the plant for a 10-year period from 1945 to 1954. The inclusion of Case 4 is warranted because of the occurrence of a new carcinoma in 1952.

The male workers in the plant may be classified in three ways: (1) The total number employed: the mean yearly population was taken as the average of the 12 monthly totals. Seasonal fluctuations were

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The occurrence of skin cancer in machine operators is of interest because of its possible relation to exposure to petroleum products, chiefly the cutting oils. When, therefore, six cases of squamous-cell carcinoma of the skin have become known at a single machine-operating plant the cases are considered of sufficient importance to warrant reporting with some observations on both clinical histories and incidence rates during the last 10 years.

The plant concerned has been in operation since before 1920. Both manual and automatic machines of different types have been used. A medical centre is maintained in the plant with a part-time physician.

It is not known if the cases reported represent all those which occurred during this period. Records are not available covering the retired, transferred, or terminated workers. There is also a possibility that cases existed for which there are no available records.

Details of these six cases (Cases 1 to 6) and of one case of skin papilloma (Case 7) are given below.

Case Reports

Case 1.—This man, born in 1896, started at the plant in 1920 as the operator of a horizontal broacher which splashed oil towards the lower abdomen of standing operators. It had been his main employment. In January, 1950, he noticed a slight chafing on the right side of the scrotum which subsequently became infected. This condition, however, was not reported to the plant physician until nearly 12 months after the initial symptom. By this time there was an indurated ulcer about 1½ in. in diameter on the right side of the scrotum with some enlargement of the lymph glands in the right groin. He was admitted to hospital and the lesion was widely excised in January, 1951. The histological diagnosis was squamous-cell carcinoma, grade III. The lymph glands in the inguinal and femoral regions were bilaterally dissected at a second operation and biopsy of these glands showed no evidence of metastatic growth. This man is still at work as a supervisor.

Case 2.—A man, born 1896, was first employed at the plant in 1935 and had operated various machines. In September, 1950, he suffered a minor laceration on the back of the right hand. A swelling, thought to be caused by an embedded steel fragment, developed at this site. It was excised about a month after the original injury. Routine biopsy examination revealed squamous-cell carcinoma, grade I. This man is still at work at the plant.

Case 3.—For 22 years this man, born in 1900, had worked as a gear cutter in another plant with similar working conditions. In 1932, while employed at this plant, he had dermatitis of both forearms. Since this time he has suffered from dermatitis of both forearms intermittently. In 1947 he transferred to the present plant. For a short time he operated automatics and later various other machines. In September, 1950, several infected papules appeared on the right forearm. One did not respond to treatment but remained as a swelling. The plant physician referred him to a dermatologist for consultation; the clinical diagnosis was epithelioma. The lesion was excised in November, 1950, and the histological diagnosis was squamous-cell carcinoma, grade I. In June, 1953, he was admitted to hospital because of traumatic pneumonitis following an injury to the chest wall. During this admission several growths of the lower abdomen and thighs were noted. One of these, a growth on the right side of the abdomen, was removed and when examined microscopically was found to be squamous-cell carcinoma, grade I. This man is still at work.

Case 4.—This man, born in 1905, began work in 1929 on the automatic machines. He had been, however, mainly occupied in other machine work. In November, 1942, he noticed a swelling on the right forearm which gradually increased in size. This was excised and microscopic examination revealed epidermoid carcinoma (low grade). In 1944 he began to suffer from recurrent dermatitis of both forearms. A dermatologist reported his condition in June, 1944, as follicular keratosis with a developing ulceration of the left forearm, clinically malignant. Radium treatment controlled this lesion satisfactorily but in follow-up visits some enlargement of

the lymph glands in the left axilla was observed. A radiologist advised excision of these glands. This was done in November, 1944. No secondary growth was observed in the dissected lymph glands. Upon recovery he returned to his former work. In 1952 a further lesion occurred on the right forearm. This was excised in December, 1952, and diagnosed as squamous-cell carcinoma, grade I. He is still at work at the plant.

Case 5.—In 1924, this worker, a man born in 1894, began as an operator on the automatic machines, later becoming a set-up man, and eventually a supervisor. In May, 1953, he reported to the medical centre with dermatitis involving both wrists and forearms. Shortly afterwards a warty growth appeared on the right wrist. This was excised in August, 1953. Microscopic examination revealed it as squamous-cell carcinoma, grade I. A second lesion occurred and was removed from the left forearm in November, 1953, with a similar histological diagnosis. He is still at work.

Case 6.—This workman, born in 1902, started at the plant in 1935 as an automatic machine operator. He suffered from an oil dermatitis in 1944 but it cleared without trouble. In July, 1952, he was seen with multiple keratoses of both forearms. These were considered clinically as precancerous lesions and removal was recommended. Several were excised in July, 1952, and were described histologically as presenting the picture of senile keratosis. Since the first excision many keratotic lesions have been removed by excision, dessication, curettage, or *x*-ray treatment. In October, 1952, a lesion removed from the left forearm showed evidence of low-grade malignancy (squamous-cell carcinoma, grade I). Numerous lesions removed subsequently from both forearms were described microscopically as oil keratosis. This man died suddenly at work in November, 1954, of heart disease.

Case 7.—This man, born in 1891, gave a history of almost unbroken employment as a machine operator since 1907. In 1925 he started to work at this plant as a set-up man on automatic machines. In May, 1945, he was seen by the plant doctor with an infected oil dermatitis of both forearms. In July of that year a consultant noted many hyperkeratotic lesions on both forearms and on the scrotum. There was a cutaneous horn on the dorsum of the right hand. At that time some of the lesions were described as potentially malignant. In October, 1945, four such lesions were excised, two from the right forearm, one from the left forearm, and one from the scrotum. Microscopic examination revealed no definite malignant change. One lesion from the right forearm was described microscopically as a papilloma and the lesion from the scrotum was described as having papillae which dipped very deeply into the corium. This workman returned to the plant after removal of the lesions. He was then given work away from oil. Despite this, hyperkeratotic lesions continued to develop and he left the plant in 1947 with the clinical diagnosis of chronic occupational dermatitis. He has been seen regularly since 1947 with a persistent dermatitis and numerous hyperkeratoses over both forearms and hands.

Observations on the Case Histories

From the data presented in Table 1 it can be seen that the age at onset of carcinoma ranges from 37 to 59 years with an average of 51.

The length of employment in the plant varied from three to 31 years. The workman who had worked only three years should rightly be excluded, since he had been similarly exposed before. When this is done the years of exposure of the remaining five cases varies from 13 to 31 years with an average period of 21 years.

TABLE 1
SUMMARY OF DATA ON PLANT CASES

Case	Machines Operated	Age at First Lesion	Plant Exposure (Years)	Original Site	Subsequent Carcinomata
1	Broacher	55	31	Scrotum	
2	Various	54	15	Right hand	
3	Various	50	3*	Right forearm	Abdominal wall (1953)
4	Various and automatics	37	13	Right forearm	Left forearm (1944) Right forearm (1952)
5	Automatics	59	29	Right wrist	Left forearm (1953)
6	Automatics	50	17	Left forearm	
7	Automatics	54	20	Right forearm	

* This man worked 22 years at similar work in previous employment.

The site of the first lesion in these cases is interesting. The exposed skin of the hand and forearm is involved in all cases except one which is of the scrotum. It is interesting also to observe that the right side is involved as the site of the first lesion in five of the six upper limb cases.

Three of the cases of carcinoma and the one case of papilloma did most or all of their work on automatic machines. Automatic machine workers comprise only about 5% of male machine operators.

The Incidence Rate

It is important to realize that in this study of the incidence of skin carcinoma the derived rates are based on only six reported cases. Furthermore, it was decided arbitrarily to study the reported cases in relation to the male population of the plant for a 10-year period from 1945 to 1954. The inclusion of Case 4 is warranted because of the occurrence of a new carcinoma in 1952.

The male workers in the plant may be classified in three ways: (1) The total number employed: the mean yearly population was taken as the average of the 12 monthly totals. Seasonal fluctuations were

not of importance in this plant. (2) The number of machine operators: the figures were obtained and handled similarly. (3) The number of machine operators employed 15 years or more: figures for these were obtained by year.

The population data for the plant are recorded in Table 2 under these three headings.

TABLE 2
PLANT POPULATION DATA 1945–1954

Year	Total Males Employed	Male Machine Operators	Male Machine Operators Employed 15 Years or More
1945	1,104	648	37
1946	1,133	687	37
1947	1,228	598	42
1948	1,351	670	47
1949	1,458	734	70
1950	1,385	701	107
1951	1,654	818	116
1952	1,498	833	127
1953	1,392	627	132
1954	1,053	543	132
Totals	13,256	6,859	847

If the six reported cases of squamous-cell carcinoma involving the limbs and scrotum are related to the total number of males employed from 1945 to 1954 the incidence rate for the plant can be expressed as 45·3 per 100,000 (standard error 18·4). Should these cases, however, be related to the machine operators only, the incidence rate would be 87·5 per 100,000 (S.E. 35·7). Five of the six observed cases occurred in machine operators employed for 15 years or more.

A comparison of the incidence of skin cancer in workers in this plant with that occurring in workers in other machine-operating plants would be of interest. Unfortunately, such figures are not available. It is possible, however, to compare the rate with that of North American males noted in Table 3. Particular attention has been given, whenever possible, to similar age groups and sites.

Included in this Table are some figures published by Jenkins (1948) on the occurrence of epitheliomata in gas and tar production workers in Great Britain. The six plant cases may be compared with eight cases, which would be expected if the crude incidence rate for Jenkins' gas and tar production workers were applied to the total number of male workers at the plant. Similarly, four cases would be expected if that rate were applied to the machine operators. If the incidence rate for carcinoma of the skin involving limbs, trunk, and scrotum in gas and tar production workers were applied to the same two groups above, one would expect three and two cases respectively. The differences between the observed number of cases and the expected numbers thus derived are not significant.

The Connecticut figures (Macdonald, 1948) reveal that 30·8% of the 2,094 male skin cancer cases reported from 1935 to 1946 occurred in the age group 30 to 59. The site distribution of these cancer cases, as well as the unpublished figures from Middlesex County and our cases are given in Table 4.

Cruickshank and Gourevitch (1952) found the scrotal and upper extremity sites to be of about equal incidence in males in Birmingham. Henry (1947) found the scrotal site to comprise 52·5% and the hand and forearm site 22·5%. His cases included many from the cotton industry. The hand and forearm site is very prominent in the plant under discussion.

TABLE 3
COMPARISON OF VARIOUS STUDIES OF SKIN CANCER INCIDENCE IN MALES*

Region	Group	Year	Cases Reported	% Biopsied	Rate per 100,000 Males	
					Skin of Limbs, Scrotum, and Trunk	All Skin
Southern United States	Birmingham, Ala.†	1948	244	66	27·7	146·7
	Dallas, Texas†	1948	329	64	23·5	138·2
	New Orleans, La.	1947	201	72	17·7	108·0
	San Francisco, Calif.	1947	683	70	16·3	95·0
	Atlanta, Ga.†	1947	234	41	4·6	35·8
Northern United States	Pittsburgh, Pa.	1947	284	83	8·6	38·7
	Philadelphia, Pa.†	1948	351	86	7·4	36·0
	Detroit, Mich.†	1948	311	74	6·8	30·0
	Chicago, Ill.†	1947	489	61	4·5	26·2
	Connecticut (Macdonald, 1948)	1940–46	‡	74	5·9	23·5
Ontario, Canada	London and Middlesex County (Sellers and others, 1950)	1939	44	52	—	71·0
	London and Middlesex County§	1953	51	93	—	60·7
	London and Middlesex, Age 15–64§	1953	10	90	1·8	18·4
Great Britain	Gas and tar production workers (Jenkins, 1948)	1933–42	22	73	24·8	60·7

* Source is the United States Federal Security Agency (1950–1952) unless otherwise noted.
† White males only.
‡ 2,094 male cases from 1935–46.
§ Unpublished figures; 1953 estimated male population 84,000.

TABLE 4
PERCENTAGE DISTRIBUTION OF SKIN CANCER BY SITE

Group and Year	Cases Reported	Upper Extremity	Lower Extremity	Trunk and Scrotum	Multiple Sites	Other Sites
Connecticut (1935–1946) (Macdonald, 1948) ..	2,094	9·6	3·4	8·7	4·0	74·3
London and Middlesex (1953) (Unpublished)	202*	1·5	3·5	4·5	2·0	88·5
Our Series (1945–1954)	6	83·3	—	16·7	—	—

* Prevalent skin cancers, including 51 new cases but excluding five melanomata.

In England and Wales, 340 cases of mineral oil epitheliomatous ulceration were recorded in the 10 years 1943 to1952 according to the annual reports of the Chief Inspector of Factories (Ministry of Labour and National Service, 1943–52). A complete breakdown of these cases by occupational group is not given in either the 1943 or the 1945 report. In the remaining eight reports, however, some 16 cases can be found which may be classified as affecting machine operators. These would probably correspond to our plant cases. A large proportion of the 340 notifications are from the cotton industry. It must be borne in mind, however, that notifications to the Chief Inspector of Factories are incomplete. Cruickshank and Squire (1950) reported a case of scrotal carcinoma in an automatic machine operator. In a study of the United Birmingham Hospitals records from 1939 to 1948 they found 34 workers with scrotal cancer, six of whom were machine operators and a further six were exposed to oil in the engineering industry. Cruickshank and Gourevitch (1952) in a continued study of hospital records noted 44 cases of epithelioma of the hands and forearm and 34 of the scrotum between 1941 and 1950. Of these, 16 hand and forearm cases and 14 scrotum cases occurred amongst metal workers. The latter 30 cases, occurring in the Birmingham area over a 10-year period, may be compared with the six cases reported here during a similar period.

The crude incidence of skin carcinoma in the total number of male plant workers and in machine operators (based on six cases over 10 years at the plant) is not remarkable compared with that of all other groups noted. But when allowance is made for age, for the site affected, and for the geographic region, these observations suggest a possible relationship between the occurrence of squamous-cell carcinoma and long-continued occupation as a machine operator. Exposure to cutting oil is likely to be the important factor.

Summary

Six histologically verified cases of squamous-cell carcinoma and one of papilloma in workers of a single machine-operating plant are reported.

Three of these cases had four new occurrences of squamous-cell carcinoma (three verified by biopsy).

The age at onset of the six cases was from 37 to 59 years with an average age of 51.

The average period of exposure for five of the six cases was 21 years (Case 3 excluded).

Automatic machine workers, who comprised about 5% of the machine operators, made up from one-third to one-half of the cases of carcinoma.

The exposed skin of the hand and forearm constituted five of the six cases of carcinoma.

Because of the possible relationship suggested above, two of the cutting oils in use were tested experimentally for their carcinogenic effect.

This study was undertaken by Drs. J. P. W. Gilman and S. Vesselinovitch and will be reported separately as Part II of this contribution.

Acknowledgment is made of the kind assistance rendered by the plant physician, the plant officials, the Workmen's Compensation Board, and the hospital staffs. Dr. L. S. Mautner, pathologist, has given of his experience and time in checking the microscopic section on each case.

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CUTTING OILS AND SQUAMOUS-CELL CARCINOMA

PART II: AN EXPERIMENTAL STUDY OF THE CARCINOGENICITY OF TWO TYPES OF CUTTING OILS*

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That mineral oils and their derivatives would induce squamous-cell carcinoma when painted on to the skin of mice was reported by Twort and Twort (1931), and in a series of other papers by these authors which have since been statistically analysed by Irwin and Goodman (1946). More recent work has demonstrated that both straight-run distillates (Woodhouse and Irwin, 1950) and high boiling point fractions of catalytically cracked petroleum oils (Smith, Sunderland, and Sugiura, 1951) may contain numerous carcinogenic hydrocarbons, although to date no pure carcinogens have been isolated from such compounds.

The literature which we have reviewed contains surprisingly few references to occupational cancers directly attributable to cutting oil exposure in the engineering industry. However, the relationship between excessive exposure to such products and a high incidence of other occupational skin diseases is well documented (Cruickshank, 1950; Shapiro, 1950).

Cruickshank and Squire (1950) have presented evidence, from both clinical observations and biological tests on mice and rabbits, implicating exposure to cutting oils as an occupational cancer hazard. A later publication by Cruickshank and Gourevitch (1952) supported this opinion. In the latter paper the authors suggested that it was quite possible that this cancer risk (exposure to cutting oils in the engineering industry) had not been long enough in existence for it to become apparent from mortality rate studies such as those of Henry (1947). It is interesting to note that in recent years the numbers and uses of the so-called "cutting fluids" have increased considerably. Such cutting fluids generally consist of a relatively stable aqueous emulsion of sulphurized petroleum oil distillates with vegetable and mineral oils in relatively small amounts and various cutting compound additives, including emulsifying, wetting, and penetrating agents. Disinfectants are also frequently added.

A preliminary report by Gilman and Vesselinovitch (1955) demonstrated that certain fractions of soluble cutting oil were capable of inducing a high incidence of tumours in the mouse. The fractions that proved carcinogenic were cut at 630, 800, and 930° F., under vacuum distillation to avoid cracking.

The present contribution is concerned with an analysis of the tumour responses obtained in several experiments involving prolonged exposure of mice to samples and dilutions of a soluble cutting oil as well as preliminary results obtained from tests using a straight cutting oil. Both of these products were cutting oils in use at the metal working plant referred to in Part I.

Cutting oils are generally sprayed in a continuous stream over the point of contact between the cutting edge of the machine tool and the metal being processed. At this point, minute quantities of the coolant are subjected to extremely high temperatures which might quite possibly cause cracking of the oils. The oil spray is collected under each machine and generally filtered through a system of weirs before returning to a sump for recirculation. Hence, one lot of oil, subject to periodic replenishment, frequently remains in use for several weeks.

Materials Tested

One of the cutting oils under investigation is marketed in the form of a water-soluble emulsion and is used in dilutions of one part to eight or more of water. As dilutions of this order might tend to obscure the presence of a weak carcinogen, tests were run using both the undiluted emulsion and various dilutions of this fluid. Samples of used cutting oils were also tested because it has been shown that cracking may greatly enhance the carcino-

* This work was supported in part by a grant-in-aid from the National Cancer Institute of Canada.

genicity of petroleum oils (Smith and others, 1951) and it seemed probable that the used oil might contain minute amounts of such cracked materials.

The properties of the two types of cutting oil and the several samples tested may be summarized as follows :

Cutting Oil A.—This is a soluble cutting fluid in the form of a stable oil-in-water emulsion containing active additives, about 45% sulphurized mineral oil base, and 40% water when marketed. It is usually diluted with eight or more parts of water before use.

Cutting Oil B.—This is a straight cutting oil, a sulphurized mineral oil blended with fatty oils. It is usually cut back with a low viscosity straight paraffin oil before use.

Samples Tested

Soluble Oil A-1-51	Undiluted ; unused (market product)
Soluble Oil A-1-53	As above—separate sample obtained over 12 months later
Soluble Oil A-2	Dilute 1 : 4 water ; unused
Soluble Oil A-3	Dilute 1 : 8 water ; unused
Soluble Oil A-4	Dilute approx. 1 : 8 water ; used*
Straight Oil B-1	Dilute 6 : 4 parts paraffin oil ; unused
Straight Oil B-2	Dilute 6 : 4 parts paraffin oil ; used.†

Methods

Samples of oil A were tested against C_3H, C_{57} black and R.F.‡ mice, while oil B was tested against C_3H mice only. Males and females were used in about equal numbers in all trials. Exposure consisted of painting the skin three times weekly with from 50 to 100 mg. of the test materials. The oils were applied with a camel-hair brush to a clipped area at the base of the neck.

Ages at the beginning of the experiments varied slightly but all groups fell within a range of from 90 to 130 days. Animals were housed in glass jars in groups of five and fed a standard commercial ration of fox cubes and rabbit pellets.

Calculations

Tumour response and carcinogenicity in this report are measured by means of the following simple statistics :—

(1) Mean Tumour Time (M.T.T.) $= \frac{\Sigma t}{TT}$

Where Σt = sum of the times in days to the appearance of the first tumour on each tumour-bearing mouse.

Where TT = total number of animals with either squamous-cell papilloma or carcinoma.

(2) Percentage tumours $= \frac{TT}{N_{corr.}} \times 100$

Where N = actual number of animals set up for each experiment.

Where $N_{corr.}$ = N less those mice that died without developing tumours before the M.T.T. minus two times its standard deviation.

(3) Percentage cancer $= \frac{C}{N_{corr.}} \times 100$

Where C = total number of mice developing histologically confirmed squamous-cell carcinoma.

(4) Mean Non-tumour Survival Time (M.S.T.$_t$) $= \frac{\Sigma t_s}{N_{nt}}$

Where Σt_s = sum of survival times in days of all non-tumour mice, those still alive at the termination of the experiment being credited with survival times equal to the duration of the experiment in days.

Where N_{nt} = number of animals that failed to develop a tumour.

The M.S.T. is accompanied by a statement of the number of non-tumour survivors at the end of the experiment and its duration in days.

Results

Table 1 summarizes the results obtained from two separate tests of sample A-1 begun 18 months apart. In each of these trials a different batch of the soluble cutting oil A was used. Of the three strains of mice exposed, the C_3H and C_{57} black were inbred stock from our own colony while the R.F. mice, obtained commercially, were not necessarily inbred.

It will be readily noticed that there was, in both trials, an appreciable difference in response between the two inbred strains. This is expressed both in the percentage of tumours and to a less marked degree in the induction period (M.T.T.).

TABLE 1

TUMOUR RESPONSE OF MICE TO SKIN PAINTING WITH A SOLUBLE CUTTING OIL AND WITH CORN OIL (CONTROL GROUP)

Sample	Strain	Number		Tumour Response			Non-tumour Mice		MST (days)
				310 Days' Exposure			End of Experiment		
		N	$N_{corr.}$	% Tumour	MTT (days)	% Cancer	Survivors	Days	
A-1-51	C_3H	20	18	61	204	22	2	401	232
	$C_{57}Bl.$	40	39	19	244	3	5	395	266
A-1-53	C_3H	30	26*	58	224	19	0	365	226
	$C_{57}Bl.$	30	30	27	255	3	1	406	256
	R.F.	30	30	33	144	7	0	310	109
Control	C_3H	20	—	0	—	0	9	401	340
	$C_{57}Bl.$	20	—	0	—	0	18	401	389

* Four deaths from injection occurred in a single cage between 161 and 175 days ; all animals showed similar necrotic liver and kidney lesions on necropsy. These four mice were discounted in calculating the response and MST.

Oil A proved highly toxic to the R.F. mice tested, with the result that this group had a non-tumour mean survival time (M.S.T.) of only 109 ± 35 days. Over 50% of the mice in this trial had died without

* Used for five weeks with daily replenishments with new emulsion

† Used for five weeks with daily replenishments with both new and reclaimed oils.

‡ Rockland Farm mice—a commercial strain of albino mice obtained from Rockland Farms, New City, N.Y., U.S.A.

having developed a tumour before reaching the M.T.T. for the group as a whole (144 days). All the R.F. mice were dead by 310 days, and for this reason length of exposure has been chosen for the comparison between samples and strains shown in Table 1. The control groups of C_3H and C_{57} black were exposed to the same treatment as the test mice, except that they were painted with a domestic corn oil.

Regardless of the differences in response of the strains, it is quite evident that cutting oil A has, for a crude commercial product, quite a high tumour-inducing potency against mice and that this response shows a high level of repeatability.

In an initial investigation, the used oil (sample A-4) had shown only a very slight carcinogenic potency (Gilman, 1950–51, unpublished data). Consequently the tests summarized in Table 2 were undertaken, making use of similar dilutions of used (A-4) and unused (A-3) materials along with an unused intermediate dilution (A-2) of one part oil A to four parts of water. It was hoped that a comparison of the results obtained with these and with the undiluted product might help to clarify the role of dilution in reducing the tumour-producing activity of the used product.

TABLE 2

EFFECT OF DILUTION ON TUMOUR RESPONSE OF C_3H MICE TO SOLUBLE CUTTING OIL A

Sample	Dilution	Numbers		Tumour Response			Non-tumour Mice		MST (days)
				365 Days' Exposure			End of Experiment		
		N	N corr.	% Tumour	MTT (days)	% Cancer	Survivors	Days	
A–1	None	30	26*	61·5	224	23·1	0	365	226
A–2	1 : 4	20	20	15·0†	291	0	3	456	323
A–3	1 : 8	20	20	0	—	0	9	456	335
A–4	1 : 8 (used)	20	20	0	—	0	15	412	396

* See footnote to Table 1.
† One of the papillomas in the 1 : 4 group regressed by 310 days.

The percentage of C_3H mice developing tumours from the 1 : 4 solution is slightly less than a quarter of that observed for the pure product, while the induction period (M.T.T.) had increased on the average about 70 days. Neither the used nor the unused 1 : 8 dilutions had elicited any response after exposure for a full year.

Mice of the apparently less susceptible C_{57} black strain were also exposed to the same dilution samples of the soluble oil as were used on the C_3H groups (Table 3). After 365 days' exposure the C_{57} group showed similar but on the whole somewhat less marked responses to the treatments.

TABLE 3

RESPONSE OF C_{57} BLACK MICE TO DILUTIONS OF SOLUBLE CUTTING OIL A

Sample	Dilution	Number		365 Days % Tumour	Response at End of Exposure Period			
		N	N corr.		% Tumour	MTT (days)	% Cancer	Duration (days)
A–1	None	30	29	41	45	255	17	406
A–2	1 : 4	20	20	5	20	408	0	456
A–3	1 : 8	20	20	0	0	—	0	456
A–4	1 : 8 (used)	40	35	3	3	—	3	395

It is interesting to note that after 456 days the 1 : 4 group showed 20% tumours, a figure only slightly in excess of the response registered by the C_3H mice after 90 days less exposure time to the same treatment.

The results recorded in Table 4 for the straight cutting oil (samples B-1 and B-2) are from a pilot test involving too few animals and too short an exposure time to warrant the making of comparisons between these and the other cutting oil samples tested. However, sample B-1 was apparently responsible for skin tumours in two of the 10 animals exposed. One of these developed into a typical squamous-cell carcinoma and eventually metastasized to the lung.

TABLE 4

TUMOUR RESPONSE OF C_3H MICE TO STRAIGHT CUTTING OIL (BLENDED 6 : 4 WITH PARAFFIN OIL)

Sample	Number		% Tumour	MTT (days)	% Cancer	Days on Experiment
	N	N corr.				
B–1	10	10	20	162	10	320
B–2	16	16	0	—	0	295

Thus it would appear that this cutting oil is also carcinogenic, although confirmation of this and detail as to potency will have to await the completion of experiments in progress.

Discussion

The oil base of the soluble cutting oil tested is a 50–50 blend of sulphurized and filtered straight-run distillates of a crude mineral oil. These base oil fractions are supposedly not cracked and contain no additives other than commercial flowers of sulphur. Thus it might be expected that oil A would give a tumour response comparable to those reported for similar straight-run distillates. However, it would appear to be considerably more potent to the mouse than the several mineral oils and fractions tested by Woodhouse (1951, 1952) and his colleagues. This discrepancy in intensity of response suggests the possibility that one or more of the additives used in compounding the cutting fluid may be acting

synergistically with the mineral oils. None of these additives have been recorded in the literature reviewed as being either carcinogens or cocarcinogens ; however, their possible role is being investigated at this laboratory.

The actual use of the cutting fluid A apparently does not either markedly reduce or enhance its tumour-producing potency. It had seemed possible that a reduction in carcinogenic activity might have been associated with oxidation of the carcinogenic components of the used oil, resulting possibly from extensive contact with metal particles. That oxidation may inhibit the potency of carcinogenic shale oil and synthetic tar has been shown by Twort and Twort (1930). However, in all probability the major part of those differences in response recorded in Table 2 is a simple function of the various levels of dilution. This contention is supported by evidence obtained from tests using C_{57}/C_3H hybrids. Such hybrids are hardy, long-lived and resistant to the toxicity of the oils, yet seemingly susceptible to their carcinogenic properties. Twenty such mice, out of C_{57} mothers and therefore free from spontaneous mammary tumours, were treated with sample A-3 (1 : 8 dilution) in exactly the same manner as the other mice reported in Tables 2 and 3 except that exposure was prolonged through a period of 525 days. At 365 and 450 days these hybrids showed no response. However, by 525 days, with all 20 hybrids still living, three had developed tumours, one of which had become cancerous, a response approximating that of the C_3H and C_{57} pure strain groups to the more concentrated 1 : 4 dilution after 365 and 456 days respectively. This suggests that, if exposure time to the various dilutions could be sufficiently extended, a tumour incidence comparable to that of the undiluted sample would ultimately be achieved. Apparently the induction period was the only variable appreciably affected by these dilutions. The advantage of using hybrid mice for testing substances that are highly toxic and where exposure may need to be continued over very long periods of time is also apparent.

These observations are of particular interest when it is remembered that it is with just such highly diluted oil-in-water emulsions that the machine operator is in contact. It is only to be expected that, if cutting oils are an aetiological factor in the occurrence of squamous-cell carcinoma amongst exposed workers, such cases will probably be preceded by long periods of exposure. It would seem then that the length of the exposure period should be considered as a very important factor in the evaluation of results of experiments, such as those reported by Smith and others (1951), concerning the effect of dilution with an inactive material on the carcinogenicity of active fractions of catalytically cracked oils. These data seemingly influenced the interim recommendation by Holt, Hendricks, Eckardt, Stanton, and Page (1951) that blends of oil containing more than 10% of catalytically cracked oil boiling above 700° F. be considered carcinogenic.

Smith and Sunderland (1951) have reported differences in the response of various strains of mice to the same carcinogen. The evidence presented in this communication clearly supports their observations (Table 1). It appears advisable, therefore, to test against more than one strain of mice when attempting to determine whether or not a substance is carcinogenic. This would seem to be particularly important if the rabbit is not available for duplicate testing, in accordance with the suggestion of Hieger and Woodhouse (1952).

The inclusion of the mean survival time of those animals that failed to develop tumours along with the number of non-tumour survivors and the duration of each trial gives some indication of the reliability of the results in terms of the toxicity of the substances tested and response of the treated mice (other than tumour development) to the conditions of the particular experiment.

Summary

A soluble cutting fluid (oil-in-water emulsion) used in industry has been shown to be carcinogenic to three different strains of mice.

The response of test groups to a standard skin painting technique varied with the strain used from 19 to 61% tumours after 310 days' exposure.

Results proved reproduceable and comparatively constant in two trials repeated after an interval of 18 months.

The responses in mice to 1 : 4 and 1 : 8 aqueous dilutions of this soluble oil were compared with the undiluted product and with a 1 : 8 used dilution after 365 days' exposure. A marked reduction in the percentage of mice bearing tumours and an increase in induction periods accompanied dilution.

Evidence was presented which suggests that the chief effect of dilution is the lengthening of the induction period. Thus when duration of treatment with a dilute oil was lengthened sufficiently the absolute tumour response approached that of mice exposed to the more concentrated emulsions.

Results of tests using a straight cutting oil (blend) are reported and suggest that this type may also be carcinogenic to the mouse.

The active interest in these investigations displayed by Dr. J. G. Cunningham (Director, Division of Industrial Hygiene, Ontario Department of Health), through whose division the original oil samples were obtained, is greatly appreciated by the authors.

We also wish to express our appreciation to Dr. J. D. Schroder of the Department of Pathology, Ontario Veterinary College, Guelph, who examined histopathologically all mouse tumour material discussed in this report.

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THE APRIL (1955) ISSUE

The April (1955) issue contains the following papers :—

Mortality from Lung Cancer in Asbestos Workers. By Richard Doll.

Primary Lung Cancer in South Wales Coal-workers with Pneumoconiosis. By W. R. L. James.

Pulmonary Fibrosis in Non-ferrous Foundry Workers. By H. E. Harding and A. I. G. McLaughlin.

Leptospiral Serology in Scottish Coal-miners. By R. S. F. Adam and P. N. Edmunds.

Diurnal Variation in Mental Performance. By Bo Bjerner, Åke Holm, and Åke Swensson.

Physiological Observations on Men Working in Supposedly Limiting Environments in a West African Gold-mine. By W. S. S. Ladell.

The Influence of Inspired Air Temperature on Tolerance to Work in the Heat. By A. R. Lind.

Investigations into the Effects of Exposure to Trichlorethylene in Mechanical Engineering. By E. Grandjean, R. Münchinger, V. Turrian, P. A. Haas, H.-K. Knoepfel, and H. Rosenmund.

Conference of the British Occupational Hygiene Society on Radiation Hazards in Industry :

The Health of Workers Exposed to Ionizing Radiations. By A. S. McLean.

Radiation Safety at an Atomic Energy Factory. By D. R. R. Fair.

Protection against *X* rays and Gamma rays in the Industrial Field. By W. Binks.

Safety Criteria in Atomic Energy. By F. R. Farmer.

Miscellanea :

Occupational Dermatitis Caused by Ethylene Oxide. By A. Royce and W. K. S. Moore.

Blood Examinations in Industry : A Comparison of Blood Cell Counts from Ear Lobe and Thumb Pulp. By A. Butterworth and N. Goodman.

Raynaud's Phenomenon. By Andrew Meiklejohn.

First Ordinary Meeting of the British Occupational Hygiene Society

Obituary : Cecil Gordon Roberts.

Books Received.

A number of copies are still available and may be obtained from the Publishing Manager, British Medical Association, Tavistock Square, W.C.1, price 12s. 6d.

Brit. J. industr. Med., 1955, **12**, 249.

RHEUMATISM IN COAL MINERS

PART III : OCCUPATIONAL FACTORS

BY

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(RECEIVED FOR PUBLICATION MAY 12, 1954)

In previous reports rheumatic complaints in miners and non-mining members of the same population have been compared. Miners lost more working time from rheumatic complaints and had more frequent and severe changes both of degeneration of the intervertebral discs and of osteo-arthritis of the knees and other joints (Lawrence and Aitken-Swan, 1952 ; Kellgren and Lawrence, 1952).

SCOPE OF THE PRESENT STUDY

In the present study an attempt has been made to discover the factors in mining which are responsible for the observed increase of disc degeneration and osteo-arthritis by investigating the relative effect of work at the coal-face and in the roadways, the effect of damp, of posture, and of heavy lifting.

Other factors which have been investigated include injury, distance walked, height of the miner, stem height, body weight, and evidence of healed rickets.

Method of Selection of Main Groups

Roadway Workers.—In Part II a random sample of underground workers between the ages of 41 and 50 employed at the Bedford Colliery in Leigh was compared with a similar sample of non-miners. As most underground workers are at the coal-face this meant that only a few of our random sample were employed on the roadways or at the pit bottom. To give a useful comparison between face and roadway workers, therefore, all remaining roadway workers within the 41 to 50 age-group at the Bedford Colliery were examined. This gave similar numbers of face and roadway workers and thus enabled a broad comparison to be made between these two main groups.

Work in Wet Conditions.—As the Bedford Colliery has for the most part been a dry mine and few of the workers had ever worked in damp either there or at the collieries round about, the survey was extended to a mine containing wet workings. It was necessary to go to the Yorkshire coalfield where, at Firbeck Colliery, water had been present in one of the workings for many years. As this seam was of similar height to those at the Bedford Colliery (3 to 4 ft.), employed the same method of working, and appeared in every other way similar, it seemed unlikely that other factors than climate would enter into any comparisons which might be made. All the workers between the ages of 41 and 50 on this face and on a comparable dry face at the same colliery were examined.

Posture.—Miners have often to adopt awkward postures while working. A stoping poosture is particularly common and might well, by throwing an additional strain on the lumbar spine, be responsible for an increased incidence of disc disorders.

During the early stages of this survey pilot studies were made in pits having varying conditions of work situated in the Lancashire area. From these it was possible to study the incidence of rheumatic complaints in men who had worked at different seam heights. It was found that rheumatic complaints reached a maximum in two peaks, one at a seam height of 3 ft. to 3 ft. 5 in. and the other at a height of 4 ft. 6 in. to 4 ft. 11 in. These peaks were not present in the younger workers but became apparent about the fourth and fifth decades and were still present in the whole group after correction for age. Loss of work from rheumatism showed a similar increase at the same two heights.

The radiological studies at the Bedford Colliery gave little information on this point, as nearly all the face workers had been accustomed to roof heights of between 3 and 4 ft., and though in the roadways the roof is higher, comparison of face and roadway workers introduces other variables and cannot be used to determine the effect of posture. A study has therefore been made of men working in seams of 4 ft. 6 in. to 5 ft. 6 in. These were available in

Walkden at both the Sandhole and Mosley Common collieries. All those at the Sandhole Colliery working at this seam height and between the ages of 41 and 50 were therefore examined, and as the numbers proved inadequate a random sample was taken of those working in the same condition at the Mosley Common Colliery. This gave a total group of similar size to that examined at the Bedford and Firbeck collieries. It was equally divided between the Mosley Common and Sandhole collieries.

Heavy Lifting.—To determine the importance of this factor a group of dock workers has been studied. This enabled comparisons to be made between heavy workers in and outside the mines, and, with the groups examined from the Walkden Engineering Yard and the National Coal Board Offices in the first part of the survey, gave a comparison of three grades of "heaviness" of work independent of mining. A random sample of 66 dockers was taken from those between the ages of 41 and 50 who had worked for 11 or more years at the docks. For the most part these were general workers of the type known as stevedores, though a few had limited themselves in earlier years to carrying timber.

Mode of Examination

The routine followed in the examination of each man has already been described in a previous paper (Kellgren and Lawrence, 1952). The radiographs of the cervical spine and hand were, however, omitted from this part of the survey and routine radiographs taken only of the lumbar spine and knees, other parts being radiographed when indicated by the clinical findings. In addition to the changes observed and noted in the first part of the survey the location of the affected intervertebral discs and the most-affected disc were also determined in each case. The radiographs were read by two observers without a knowledge of the individual's occupation or of his symptoms or physical findings. The criteria used for grading radiological changes are those already laid down in the above paper. (The problem of observer error in reading radiographs is discussed in the appendix.)

RESULTS

Although the lumbar spine and knees have been studied in equal detail the spine will have a greater place in the results which follow as the investigation into factors causing knee symptoms proved less informative.

Spine

The cervical spine has been dealt with in a previous report (Kellgren and Lawrence, 1952) and, as no further information is available from the present study, it will not be considered here.

The dorsal discs may be dismissed briefly as radiographs were not taken with the specific purpose of showing them and information is therefore only available on those discs which were visible in the lumbar radiographs, usually the eighth to the eleventh (the twelfth dorsal disc was included with the lumbar discs). Only three (7%) of the office workers showed radiological changes in these lower dorsal discs, and eight (18%) of the light manual workers. By contrast, changes were found in 26% of the Bedford face workers, 40% of the Bedford roadway workers, 46% of the Mosley Common and Sandhole workers, and 50% of the Firbeck men and dockers. The changes were generally classified as slight; only in some 10% were they considered severe. Nor did the number of discs affected vary markedly from group to group, but 8% of the Mosley Common and Sandhole workers and 6% of the roadway workers showed changes in three or more discs.

It may be concluded that the lower dorsal discs are more affected in those engaged in mining and other heavy work. In this respect they behave in the same way as the lumbar discs as will be shown subsequently.

Possible causative factors of lumbar disc degeneration may be divided into two main groups: (1) occupational, *e.g.*, type of work, climate, and position at work, and (2) personal, *i.e.*, body build and previous injury or disease. The occupational factors may be considered either from the qualitative or quantitative aspect, *e.g.*, the heaviness of the work and the number of years during which heavy work has been practised, the degree of stooping, and the number of years worked in a stooping position. The qualitative side is best exemplified by a comparison of the main occupational groups and these will first be considered.

Symptoms, Incapacity, and Radiological Changes According to Occupation.—There are four main occupational groups in this survey: miners, dockers, light manual, and office workers (Table 1 and Fig. 1). The miners are subdivided into roadway and face workers and the latter into three subgroups, the Bedford face workers (low roof and dry workings), the Firbeck face workers (low roof and wet conditions), and the Sandhole and Mosley Common face workers (high roof and dry conditions). There are thus seven groups in all.

The Bedford face workers have more radiological changes assessed as severe, 16% against 10%, than the Bedford roadway workers; but the difference is small and not significant ($P > 0{\cdot}2$), and the total with radiological change is almost identical (95% and 96%); nor are there significant differences

between face and roadway workers in any other respect.

This is in marked contrast to the light manual or office workers, particularly the latter in whom severe disc changes were not seen. Some roadway workers had perhaps served at the face in the past and been transferred to the roadways because of disability caused by a spinal disorder. It is, in fact, known from our records that of the 50 roadway workers at least 33 had served at the face at some time, and 15 had more experience of face than of roadway work. It is thus difficult to exclude coal-face conditions as a factor even in the disc disorders of roadway workers. It is clear, however, that severe spinal changes are common to all miners.

The dockers, although they complain as frequently of low back sciatic pain, lose work to roughly the same extent and have radiological changes as often, do not show the same grade of severity in the radiological change as the miners and fewer discs are involved, both these differences being significant. Thus, whereas 12% of miners show the highest grade of radiological change only 2% of dockers fall into this category ; 36% of miners show involvement of four or more discs, but only 18% of dockers are affected to this extent. The dockers on the other hand are considerably worse off than the light manual workers,

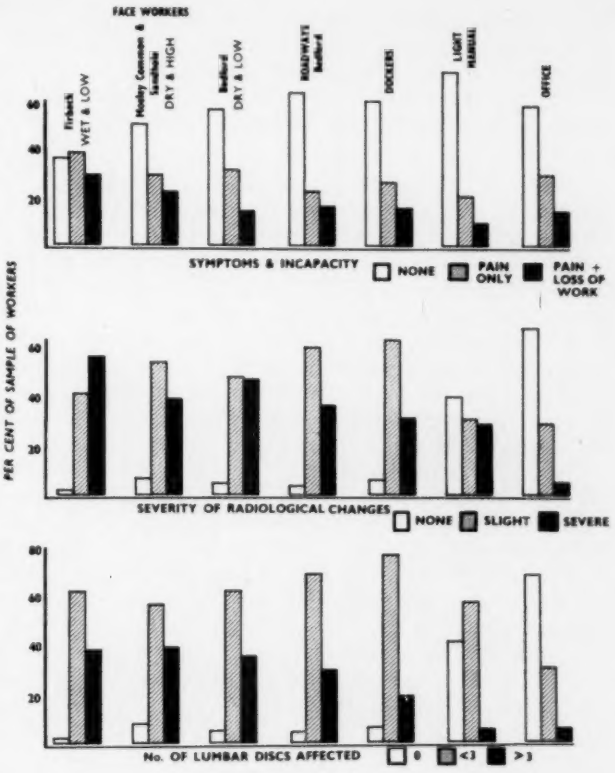

FIG. 1.—Spinal pain and radiological changes in main occupational groups. In the diagrams the doubtful and minimal radiological changes are grouped together as slight and the moderate and severe as severe.

TABLE I

SPINAL PAIN, INCAPACITY, AND RADIOLOGICAL * CHANGES IN PRIMARY GROUPS OF WORKERS

	Miners				Non-miners		
	Face Workers			Roadways	Heavy Manual	Light Manual	Sedentary
	Firbeck	Mosley Common and Sandhole	Bedford	Bedford	Dockers	Walkden Yard	N.C.B. Offices
Total men	46	61	64	50	54	45	42
Back-hip-sciatic pain	30 (65%)	31 (50%)	29 (45%)	19 (38%)	22 (41%)	13 (29%)	18 (43%)
Off work 1 week or more	13 (28%)	13 (21%)	9 (14%)	8 (16%)	8 (15%)	4 (9%)	6 (14%)
Off work 3 months or more	7 (15%)	5 (8%)	2 (3%)	3 (6%)	2 (4%)	0 (0%)	1 (2%)
Radiological changes :							
None	1 (2%)	4 (7%)	3 (5%)	2 (4%)	3 (6%)	18 (40%)	28 (67%)
Doubtful	0	7	7	6	11	4	4
Minimal	19 (41%)	26 (54%)	24 (48%)	24 (60%)	23 (63%)	10 (31%)	8 (29%)
Moderate	20	19	20	13	16	12	2
Severe	6 (56%)	5 (39%)	10 (47%)	5 (36%)	1 (31%)	1 (29%)	0 (5%)
No. of lumbar discs affected † :							
1–3	28 (61%)	34 (56%)	39 (61%)	34 (68%)	41 (76%)	25 (56%)	12 (29%)
Over 3	17 (37%)	23 (38%)	22 (34%)	14 (28%)	10 (18%)	2 (4%)	2 (5%)

* The radiological findings in all Tables included in this report are the mean readings of two observers and are not, therefore, identical with those given in the earlier report where the radiological readings of the senior observer were used.

† In this Table, and those which follow, the disc between D.12 and L.1 vertebrae has been included as one of the lumbar discs.

having greater disability and more frequent radiological changes. However, when radiological changes are present in the light manual workers they are just as severe as in the dockers, the difference being rather in the numbers with doubtful or minimal changes.

There are definite differences between the face workers at Bedford and Firbeck. Fewer men at Firbeck are symptom-free and loss of work is twice as frequent. Moreover, prolonged disability is five times as common in the Firbeck men. Radiological changes are absent or doubtful in only one (2%) of the Firbeck workers but in 10 (16%) of the Bedford men, a significant difference ($P<0.05$). The radiological changes are for the most part of moderate severity but it was found that they affected on an average three discs as against two in the Bedford workers. It may be concluded that the Firbeck men have more frequent involvement of discs and that these are more often of moderate severity and less often minimal. Men from the wet and dry seams at Firbeck have not been analysed separately in Table 1 as it was found that the differences in pain and disability were not striking and that in fact there had been much interchange of workers between the seams so that almost all had worked in wet conditions at some time.

The group of men from the Mosley Common and Sandhole collieries were working in dry conditions at a roof height of 4 ft. 6 in. to 5 ft. 6 in. They were thus in a similar climate to the Bedford workers but had to adopt a stooping position and did not kneel. They complained rather more than the Bedford workers of back-hip-sciatic pain, had 50% more incapacity, and nearly three times as much prolonged disability. The radiological changes, however, were no greater and the number of discs affected was also very similar.

To elucidate this further, all face workers who had not worked in wet conditions were divided up according to the predominant roof height at which they had worked (Fig. 2), *i.e.*, the height of roof at which the miner had worked for the greatest time and not necessarily the height at which he was working at the time of the survey. This confirmed previous findings as to symptoms and loss of work. Radiological changes were also most frequent in those working at a roof height up to 3 ft. 5 in. and least common in those working at 4 ft. to 4 ft. 5 in. The most severe changes, however, were found in both these groups. There were no consistent differences in the number of discs affected at different seam heights. The radiological differences were below accepted levels of significance and gave no clear evidence that there is a pathological basis for the increased disability at these roof heights though they certainly do not exclude such a basis.

The distribution of affected discs in the main occupational groups has been considered from two points of view : (1) the worst affected disc and (2) the number of instances in which each disc is affected.

TABLE 2

AFFECTED LUMBAR DISCS IN MINERS, DOCKERS, LIGHT MANUAL, AND OFFICE WORKERS*

	Bedford Miners		Firbeck	Mosley Common and Sandhole	Dockers	Light Manual	Office
	Face	Roadway					
Total men	64	50	46	61	54	45	42
Total men with abnormal discs ..	61	48	45	57	51	27	14
Worst affected disc :							
D.12	4	3	1	6	7	3	—
L.1	5	5	3	5	4	3	—
L.2	8	13	11	6	13	6	1
L.3	21	18	16	25	21	7	6
L.4	13	5	12	8	3	5	5
L.5	10	4	2	7	3	3	1
Not known	0	0	1	0	0	0	1
All affected discs :							
D.12	19	15	14	16	15	6	0
L.1	23	18	23	24	17	9	3
L.2	34	33	36	32	35	13	7
L.3	54	43	43	46	39	17	10
L.4	43	28	31	39	27	10	7
L.5	19	10	7	14	7	4	2
L.6	0	0	0	0	0	0	0
Not known	1	0	1	0	0	0	1
Total discs	192	147	154	171	140	59	29

* The results in this Table are taken from the readings of a single observer.

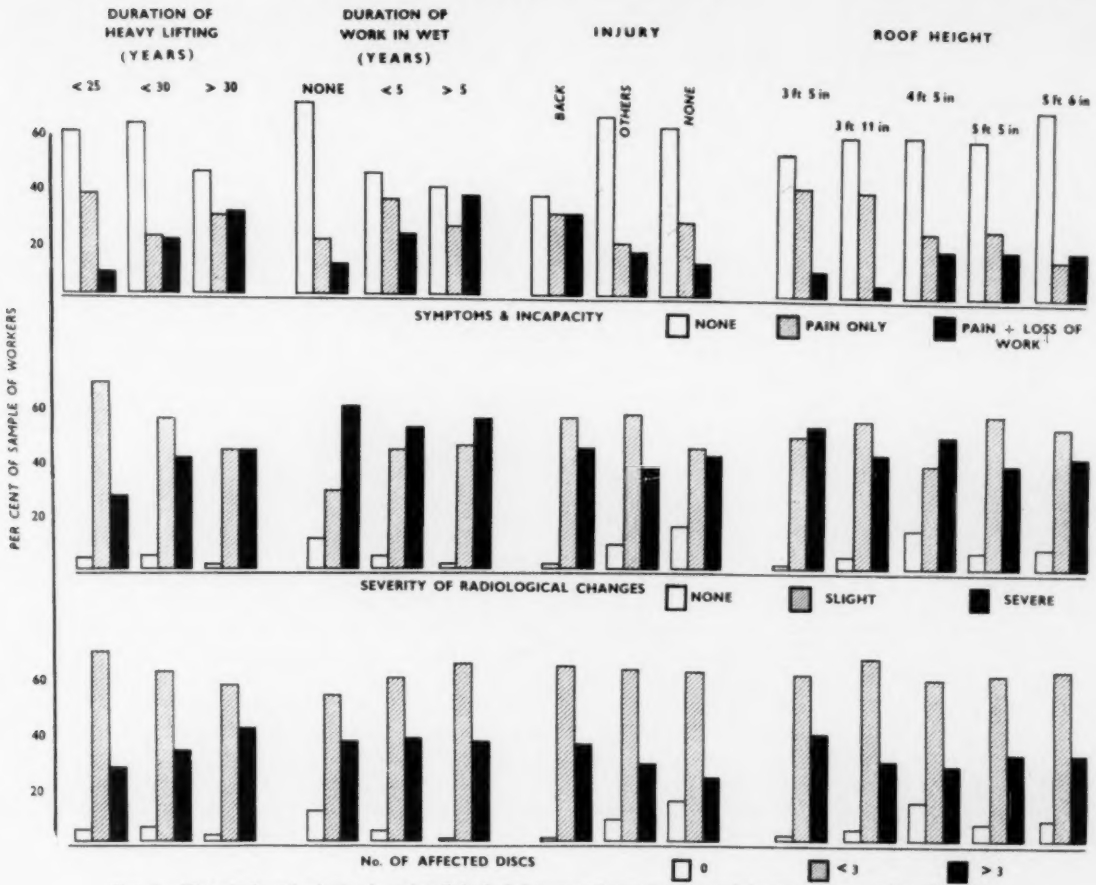

FIG. 2.—The relation of spinal pain and radiological changes to heavy lifting, work in wet, injury, and roof height.

In each of the main occupational groups (Table 2) the third lumbar disc is not only the one most frequently affected but it is most often the worst affected, and there is a fairly even distribution about this level. The distribution does, however, show less scatter in the Mosley Common and Sandhole workers in whom there is a sharper peak for the worst affected disc at L.3 as though in the position in which these men worked the brunt of the strain fell more heavily on this disc. The differences in distribution, however, are no greater than might be due to chance and with the numbers studied are only suggestive. A similar peak distribution is found also in the office workers, whose posture at work may well be comparable. The majority of them show either the third or fourth lumbar disc most affected, and none shows the greatest changes in D.12 or L.1, whereas in 22% of the light manual workers these discs are the worst affected, a significant difference ($P=0{\cdot}01$). When, instead of the worst, all affected discs are considered the conclusions are similar, for example, D.12 being quite unaffected in the office workers. Face workers tend to have the lower discs (L.4 and L.5) more affected than the roadway workers, dockers, or light manual workers, and in this respect they resemble the office workers, but this is not a significant difference and it cannot be said that the distribution of affected discs gives any indication as to causative factors in these groups.

Time Study of Occupational Factors.—The occupational factors which have been studied from this point of view are heavy lifting, work in wet, at the coal-face, and in a stooping position. Although in such studies age is commonly a factor, in this instance it can be ruled out. All the men were in the fifth decade and within this decade no age differences in relation to radiological changes were found to exist.

TABLE 3

RELATIONSHIP OF HEAVY LIFTING* TO SPINAL PAIN, INCAPACITY, AND RADIOLOGICAL CHANGES IN MINERS AND DOCKERS

Duration of Lifting in Years	−25	−30	30+
Total Men	45	64	56
Back-hip-sciatic pain ..	19 (42%)	25 (39%)	32 (57%)
Back-hip-sciatic pain, off work 1 week or more	3 (7%)	12 (19%)	16 (29%)
Back-hip-sciatic pain, off work 3 mths or more	1 (2%)	2 (3%)	9 (20%)
Radiological changes :			
None	2 (4%)	3 (5%)	1 (2%)
Doubtful	8 (67%)	8 (55%)	4 (44%)
Minimal	22	27	21
Moderate	11 (29%)	21 (41%)	24 (44%)
Severe	2	5	6
No. of lumbar discs affected :			
1	4	4	4
2	16 (69%)	15 (62%)	12 (57%)
3	11	21	16
4	8	18	14
5	3 (27%)	3 (33%)	7 (41%)
6+	1	0	2

* Information on heavy lifting was not obtained until the second half of the survey.

Heavy Lifting.—The relationship of heavy lifting to spinal pain, incapacity, and radiological changes is shown in Fig. 2 and Table 3. Only the duration of heavy lifting is considered. The actual weight lifted, the degree of strain on the structures of the back, and the continuity of such strain have not been investigated except in so far as they vary in the main occupational groups studied.

An increase of symptoms is found only in those who have carried out heavy lifting for more than 30 years, but is not significant ($P>0{\cdot}1$). Incapacity for work, however, becomes progressively greater as the duration of heavy lifting increases, and in those who have lifted for more than 30 years it is four times as great as in those who have lifted for less than 25 years. Prolonged disability (three months or more) from spinal pain also increases, being recorded in only 2% of those who have lifted for less than 25 years but in 20% of those who have been engaged in such work for more than 30 years.

The proportion showing no radiological change is small in all groups, but there are progressively fewer minimal and more numerous severe changes with increasing experience of heavy lifting, the difference between the first and last groups being significant for the most severe changes ($P<0{\cdot}02$). The number of affected discs also shows a progressive increase as the duration of heavy lifting rises. These findings are not due to an admixture of dissimilar groups. A separation of miners from dockers showed that the relationship of heavy lifting to radiological changes occurred in both groups though more marked in miners.

TABLE 4

RELATIONSHIP OF DURATION OF WORK IN WET CONDITIONS TO SPINAL PAIN, INCAPACITY, PHYSICAL SIGNS, AND RADIOLOGICAL CHANGES IN FACE WORKERS

	No Work in Wet	Work in Wet −5 Years	Work in Wet 5 Years +
Total Men	45	82	31
Back-hip-sciatic pain ..	14 (31%)	46 (56%)	19 (61%)
Back-hip-sciatic pain, off work 1 week or more..	5 (11%)	18 (22%)	11 (36%)
Back-hip-sciatic pain, off work 3 mths or more	4 (9%)	6 (7%)	4 (13%)
Physical signs : Lumbar spine, limitation ..	14 (31%)	39 (48%)	19 (61%)
Radiological changes :			
None	5 (11%)	3 (4%)	0 (0%)
Doubtful	8 (29%)	3 (44%)	2 (45%)
Minimal	15	33	12
Moderate	11 (60%)	33 (52%)	13 (55%)
Severe	16	10	4
No. of lumbar discs affected :			
1	6	6	1
2	14 (53%)	14 (60%)	11 (65%)
3	4	29	8
4	9	17	7
5	5 (36%)	10 (37%)	4 (36%)
6+	2	3	0

Work in Wet.—In Table 4 and Fig. 2 the relationship of work in wet to symptoms, signs, and radiological changes is analysed. Only face workers have been used for this analysis as it is desired to eliminate other variables as far as possible. These workers have been divided, regardless of the colliery in which they worked, into those who have not been in wet and those working for varying periods in wet conditions. The information is derived from the man's statement and is thus dependent on memory. An element of bias cannot, therefore, be entirely excluded, but in view of the negative correlation with knee pain, which will be referred to later, it would seem improbable that such a bias has played an important part.

The relationship of work in wet to symptoms is quite striking. There is an increasing incidence of back-hip-sciatic pain so that those working for more than five years in wet have twice as high an incidence as those who have always worked in dry conditions. This difference is significant ($P<0{\cdot}05$). Similarly, loss of working time from back-hip-sciatic pain shows a step-by-step relationship with work in wet, and is three times as frequent in those who have worked for more than five years in wet conditions. Prolonged disability, however, shows no clear relationship but physical signs in the spine are related in the same way as symptoms.

The incidence of radiological changes in the spine shows a similar progressive relationship to work in wet, and, indeed, none of those who have worked for more than five years in wet has a normal spine compared with 11% of those who have not worked

in wet. Doubtful changes similarly are more frequent in the dry workers whereas the wet workers have more minimal and moderate changes. This is offset, however, by the most severe changes which are most frequent in the dry workers ($0{\cdot}1 > P > 0{\cdot}05$). A study of the number of affected discs shows no significant relationship to work in wet conditions.

It may be concluded that work in wet is associated with a disproportionate increase of pain and disability, and that radiological changes in such workers, though they may be more frequent, are unlikely to be severe.

Duration of Work at Face in Miners.—In view of the similar incidence of both spinal pain and radiological changes already noted between face and roadway workers, it is not surprising that no constant relationship to the duration of work at the face was found. Back-hip-sciatic pain appeared to be entirely independent of the time worked at the face, and the proportion losing working time also showed no constant relationship. Prolonged disability was four times as common in those who had worked over 30 years at the coal face, and this difference was highly significant ($P < 0{\cdot}01$). The radiological changes on the other hand showed no definite trend. It was, however, noticeable that those who had had a variety of jobs fared better in this respect than those who had remained all the time either in the roadways or at the face. It should be pointed out that those who remained all the time in the roadways were generally concerned with development work, a task which involves much heavy lifting.

Duration of Stooping.—Pain was most frequently present in men who had worked from 15 to 25 years in a stooping position. Those who had stooped less or more than this, less often complained. Loss of work and prolonged disability were also greater in this group. The physical signs, on the other hand, particularly limitation of straight leg raising, became less with prolonged stooping, but radiological changes became increasingly severe and involvement of multiple discs increasingly more probable. The increase of severity, however, was not marked and was within the limits of chance, but there were significantly more men with five or six discs involved amongst the prolonged stoopers (over 30 years $P = 0{\cdot}02$).

Prolonged stooping thus appears to have an adverse effect on the intervertebral discs but there is some measure of adaptation with persistence at this type of work. The alternative that those most susceptible to pain go over to work of a different nature and so do not develop such severe changes must, of course, be considered. In either event it would appear that prolonged stooping is one of the factors in mining which tends to increase the severity and frequency of disc changes.

Personal Factors.—The following personal factors possibly causing lumbar disc degeneration have been studied.

Injury to Back.—In those with a history of injury to the back (Table 5 and Fig. 2), pain in the back-hip-sciatic distribution is almost twice as common as in those without such a history, and incapacity and prolonged disability are also twice as great. Those who have had an injury to some other part do not show this high incidence of pain and incapacity. Radiological changes are absent in only one man (1%) with a history of back injury but in 8% of those with other injuries and 15% of those without a history of injury. All these differences are significant ($P = 0{\cdot}05$). The radiological changes are not, however, more severe in those who have suffered a back injury, though multiple disc involvement is more likely. The pattern of disc involvement was similar in those with and without injury, the third lumbar disc being most affected in each group and there was no indication that injury was associated with a different type of disc degeneration.

These figures, of course, cannot be accepted without reserve. It must be considered first whether an injury to the back is more likely to be remembered by a man with pain in the back, particularly if associated with loss of work, and whether such men are more likely to have radiological changes.

TABLE 5

RELATIONSHIP OF SPINAL PAIN, INCAPACITY, AND RADIOLOGICAL CHANGES TO A HISTORY OF BACK INJURY IN MINERS AND OTHER MANUAL WORKERS

	Back Injuries	Other Injuries	No Injuries
Total Men 289	75 (26%)	86 (30%)	128 (44%)
Back-hip-sciatic pain ..	48 (64%)	30 (35%)	50 (39%)
Back-hip-sciatic pain, off work 1 week or more..	24 (32%)	14 (16%)	15 (12%)
Back-hip-sciatic pain, off work 3 mths or more	8 (11%)	5 (6%)	5 (4%)
Radiological changes :			
None	1 (1%)	7 (8%)	19 (15%)
Doubtful	7 (55%)	12 (56%)	13 (44%)
Minimal	34	36	44
Moderate	24 (44%)	26 (36%)	42 (41%)
Severe	9	5	10
No. of lumbar discs affected :			
1	8	8	12
2	17 (64%)	27 (63%)	29 (62%)
3	23	20	38
4	16	15	18
5	8 (35%)	9 (28%)	9 (23%)
6+	2	0	3

To determine these points a sample of 100 men was taken and details of the injuries received were collected from the colliery records, comparison being made with the accidents remembered at the time of interview. It was found that although in some instances injuries were forgotten and in others men stated that they had had injuries which were not found in the records (presumably sustained while working at other collieries), there was very substantial agreement between the remembered and recorded injuries. Nor did those with pain prove to have better memories than those without ; quite the reverse was, in fact, found.

Whatever the part played by injury in causing disc degeneration it is clear that injury, at least as defined by the colliery records, is not the only factor. Only 28% of those with definite radiological changes gave a history of back injury.

Other Personal Factors.—The remaining personal characteristics of the miner—height, stem height, and old healed rickets as evidenced by genu varum—have not appeared to play an important part in determining the onset and progress of disc degeneration. The taller men more often complained of back-hip-sciatic pain and had more severe radiological changes and where the increased height was due to a long back they suffered greater incapacity. Those with genu varum also had more frequent pain and lost more work but did not show greater radiological change.

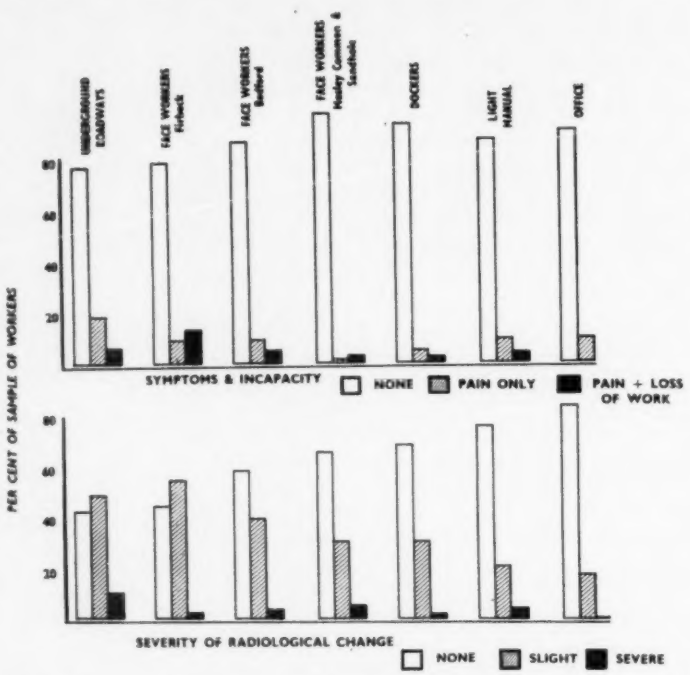

FIG. 3.—Knee pain, physical signs, and radiological changes in main occupational groups.

Knees

The incidence of knee pain (Table 6 and Fig. 3) differed considerably in the groups studied. It was

TABLE 6

KNEE PAIN, INCAPACITY, PHYSICAL SIGNS, AND RADIOLOGICAL CHANGES IN MINERS, DOCKERS, LIGHT MANUAL, AND OFFICE WORKERS

	Bedford Face	Bedford Roadways	Mosley Common and Sandhole	Firbeck	Dockers	Light Manual	Office
Total men	64	50	61	46	54	45	42
Knee pain	9 (14%)	12 (24%)	2 (3%)	10 (22%)	4 (7%)	6 (13%)	4 (10%)
,, ,, off work one week or more	3 (5%)	3 (6%)	1 (2%)	6 (13%)	1 (2%)	2 (4%)	0 (0%)
,, ,, off work three months or more	0 (0%)	1 (2%)	0 (0%)	3 (7%)	0 (0%)	1 (2%)	0 (0%)
Physical signs	18 (28%)	15 (30%)	14 (23%)	11 (24%)	10 (18%)	8 (18%)	10 (24%)
Radiological changes :							
None	37 (58%)	21 (42%)	40 (66%)	20 (43%)	37 (68%)	34 (76%)	35 (83%)
Doubtful	16 (25%)	11 (22%)	9 (15%)	12 (26%)	11 (20%)	6 (13%)	4 (10%)
Minimal	9 (14%)	13 (26%)	9 (15%)	13 (28%)	5 (9%)	3 (7%)	3 (7%)
Moderate	2 (3%)	5 (10%)	2 (3%)	1 (2%)	1 (2%)	2 (4%)	0 (0%)
Severe	0 (0%)	0 (0%)	1 (2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Total with radiological changes	27 (42%)	29 (58%)	21 (34%)	26 (57%)	27 (32%)	11 (24%)	7 (17%)
Total with definite radiological changes	11 (17%)	18 (36%)	12 (20%)	14 (30%)	6 (11%)	5 (11%)	3 (7%)

greatest in the underground roadway workers, the face workers having less but showing great variation in different mines. For example, amongst face workers in the wet Firbeck mine, knee pain was almost as frequent as in the roadway workers at Bedford, but in the high seams at the Mosley Common and Sandhole collieries the incidence was low. The light manual and office workers and the dockers occupied an intermediate position, the dockers complaining least. The proportion losing work was similarly distributed except that the Firbeck miners suffered relatively more incapacity.

The radiological changes showed quite marked variation between the groups, following closely the incidence of symptoms. Thus the roadway workers showed the highest incidence, 36% having definite evidence of osteo-arthritis. Next in frequency came the Firbeck miners and then the other face workers. The difference between the face and roadway workers is just significant ($P=0{\cdot}05$). The dockers and light manual workers showed less radiological evidence, and of the office staff only 7% had definite changes. Both the face and roadway workers had significantly more radiological change than the office workers, but the dockers and light manual workers did not differ significantly from the office staff.

It may be concluded that there is some factor in mining which is not present in dock or light manual work and which results in an increased incidence of osteo-arthritis of the knees. This has been investigated from several angles—kneeling, walking, injury, exposure to wet, and heavy lifting, also personal factors such as body weight or faulty mechanics due to pre-existing deformity.

Kneeling was not found to be a factor and indeed knee pain and incapacity so arising were more frequent in those who had worked predominantly in the higher seams of over 4 ft. Radiological changes in the knees were unaffected either by the duration of kneeling or the seam height.

Only a few of the men gave a history of injury to the knee, but it was evident that when this did occur it was a potent source of osteo-arthritis. Despite the small number involved the increase of symptoms, loss of work, physical signs, and radiological changes were all significant. This accounted for only a very small proportion of the osteo-arthritis found in the knees. Whether minor injuries which had been forgotten or had not been thought worth reporting could have been responsible for all the osteo-arthritis is uncertain. The injuries to the knee recorded were roughly equally divided between strains and blows.

There was no evidence of any relationship of distance walked at work to knee complaints or radiological changes, nor did it appear that heavy lifting or the duration of work in wet was an important factor in osteo-arthritis of the knees.

There were virtually no really obese men in this survey, but within the range encountered there was no evidence of any relationship between body weight and pain, loss of work, or physical signs. Radiological changes in the knees, however, showed a close relationship, being progressively more common with increase of body weight. It was, however, chiefly the doubtful and minimal radiological changes which were so influenced.

Those with a definite degree of genu varum (over 2 cm.) complained rather more often of pain in the knee and more often lost time from work, which was usually prolonged. There was also a rather higher incidence of radiological changes in this group but the increase was not significant. Thus, though it cannot be denied that genu varum may increase to some extent a tendency to osteo-arthritis of the knees, it cannot be said that it bears an important causal relationship.

Other Joints

Of the remaining joints the elbow was most frequently affected, the highest incidence being in the workers at Firbeck. The roadway workers at Bedford, however, showed almost as much, but there was a lower incidence at Mosley Common, at Sandhole, and at Bedford coal-face. The dock workers had roughly the same proportion as the Bedford face workers. No osteo-arthritis of the elbow was encountered amongst the light manual and office workers.

The possibility was considered that in miners the use of a pneumatic drill might be responsible, and altogether 177 men were asked about drilling. Of those who had not drilled, 22 (16%) were found to have osteo-arthritis of the elbow, whereas of 39 who had drilled for more than a year 12 (31%) were affected. The numbers, however, are small and the difference is not statistically significant. It is apparent that osteo-arthritis often occurs in those who have done no drilling, and is, moreover, a feature of all heavy work studied.

Osteo-arthritis of the remaining joints was relatively less common.

Other Rheumatic Pains

Disc prolapse was diagnosed in seven men; in six it was situated in the lumbar spine, in one it was cervical. No conclusions as to occupational influence could be drawn.

Only four examples of rheumatoid arthritis were encountered in the survey; two of these were

light manual workers and two miners. This incidence of 1% thus corresponds with our finding of a 1·4% incidence in males of this age group in the Leigh survey of the general population.

Spondylitis and gout were not encountered, as might be expected, in view of their low incidence of approximately one per thousand.

The remaining examples of skeletal pain were of a less defined character and have been labelled "undetermined". The most frequent sites of this pain were in the dorso-pectoral or cervico-brachial distribution, but a large number were lumbar. The commonest single site was the region of the deltoid muscle. Both the dorso-pectoral and deltoid pain were encountered most often in dock workers. The cervico-brachial pain, on the other hand, was more common in the Firbeck miners and the lumbar pain in the Bedford face workers who also complained more of scapular and interscapular pain. Ankle and foot pain was a feature rather of work in the underground roadways, where also there was more complaint of multiple pains. These occupational differences are not large and none differs significantly from the mean value.

DISCUSSION

The main feature of this survey has been the high incidence in coal-miners of degenerative changes in the lower dorsal and lumbar intervertebral discs and the high proportion losing work because of corresponding lumbar and sciatic pain. It is important, therefore, to decide how this is caused and what measures, if any, can be taken to prevent the onset of these changes or of the disabling symptoms with which they are commonly associated. Factors influencing these changes may be divided into those acting on the discs themselves and those which affect symptomatology and, still more important, incapacity. A factor which affects disc change will in general also increase symptoms and incapacity but the reverse need not follow.

Trauma

The importance of trauma in disc degeneration has long been recognized. A compression fracture of the spine is nearly always associated with gross changes in the discs, and disc degeneration often follows injury which is insufficient to damage the bony structures or results only in a small chip fracture of the anterior border of one of the vertebral bodies or slight damage to the vertebral plate (Schmorl and Junghanns, 1951). Injury is unfortunately an outstanding feature of work in the mines, and though in recent years the incidence of serious or fatal accidents has been reduced, the accident rate is still very much greater in the mines than in factories (Ministry of Fuel and Power, 1953; Ministry of Labour and National Service, 1953). A feature of mining, as of other heavy occupations such as dock work, is, as our figures show, the high proportion of back injuries and the association of those with degenerative changes in the discs. It may be considered whether certain "strains" to the back are symptomatic rather than causative as obviously a man with disc degeneration will be more susceptible to strain than a man with a healthy spine. It was found, however, in this survey that radiological changes were increased almost to the same extent in those giving a history of a blow on the back and in those in whom the injury was described as a strain. It would thus appear improbable that the injury was merely a "symptom" of pre-existing disease, though in many instances pathological changes undoubtedly preceded the injury.

But though radiological changes are more frequent and more severe in those with a history of injury, they are nevertheless quite considerable in those without such a history, and miners in this category still have more radiological change than, for example, manual and office workers. An injury might of course have been forgotten by these men, but when data are obtained quite independently from the colliery records a high incidence of radiological change is still found in the uninjured. Moreover, these records include not only severe injuries qualifying for compensation, but also relatively minor injuries not associated with loss of working time. Admittedly these records cannot be complete, as many minor accidents must remain unreported and others may have been sustained during employment at another colliery. Nevertheless, it would seem unlikely that a definite injury is responsible for all cases of disc degeneration. It may be, of course, that very minor injuries, if repeated on frequent occasions, will operate in a similar manner. This was suggested as long ago as 1928 by Schmorl, and Lindblom (1952) has since shown that even continuous slight pressure may cause disc degeneration with rupture of the annulus fibrosus. Such injuries are implied in the expression "heavy lifting" and in the heaviness of the occupation in general.

Heavy Lifting

This may be measured in a number of ways as, for example, the weight lifted, the height to which it is raised, and the duration and frequency of such incidents of lifting. It may be expressed as the number of years during which a man has engaged in heavy lifting. Only the last can be assessed with

any degree of precision in miners or dockers. Some measure of the former might be obtained either by job analysis or by quantitative electromyographic studies made while carrying out the work, but before this could be done it would be necessary to know what effect each individual task might have on the incidence of disc changes. It has not been possible to make a detailed study of this in miners as the occupations encountered in mining are so many and varied, and the numbers in each relatively small. It has, however, been possible to assess men engaged in the two main occupations, those of collier and ripper, and it was found that the men in each of these groups had more disc degeneration than other miners, the colliers showing more instances of the most severe forms of disc degeneration than the rippers. The work of a collier would thus be suitable for comparison with dockers and other manual workers on the lines indicated above, and inquiries are at present under way with a view to obtaining some measure of the stresses involved. It would seem reasonable to suppose that the order of severity—in miners, dockers, light manual, and office workers—indicated by this radiological study corresponds with the heaviness of the task involved.

This is confirmed to some extent by the incidence of chip fractures of the vertebral bodies and of herniation of disc substance through the intervertebral plates (Schmorl's nodes). One or other of these was encountered in 6% of miners, 4% of dockers, 1% of light manual workers, and in none of the office workers. These changes indicate only a single severe strain. There can be little doubt that repetition, perhaps of relatively minor strains, plays just as important a part. This is indicated in miners and dockers by the relationship of spinal symptoms and signs to the duration of heavy lifting; this is closer than to any of the other possible causative factors.

Position at Work

Much importance has been attached in the past to the position of the back when lifting heavy weights, and data from the earlier survey appeared to indicate that this was a factor in mining as pain and disability were greatest in those working at seam heights which involved most stooping. The radiological changes found in this part of the survey, although they suggest a greater severity at these critical seam heights, are not sufficiently marked to be significant with the small number of men involved, and we are thus unable to provide definite evidence on the point. It is apparent, however, that this is not so important a factor as injury and heavy lifting.

Damp

The effect of wet conditions, though quite definite, is more difficult to explain. From the findings in the previous survey it was clear that miners working in wet more often had symptoms attributable to lumbar disc degeneration, but it was felt that this might be due to a lowering of the pain threshold rather than to increased tissue change. This may well be a factor in view of the disproportionate incidence of symptoms and incapacity in those working in wet. Thus twice as many Firbeck miners lose work from back-hip-sciatic pain and there are also more with milder symptoms not giving rise to incapacity. Such a finding would be expected in view of the known effect of cooling on deep pain (Kellgren, McGowan, and Hughes, 1948), and this would also explain the relatively mild character of the radiological changes in those who have worked in wet, for the heightened pain sensibility would tend to have a protective effect. It does not, however, explain the more frequent radiological changes in miners.

In view of the influence of heavy lifting and injury to the back on disc changes, it must be considered whether these are operative to a greater degree in men working in wet conditions. A higher accident rate in wet workings might account for the increased radiological changes but, in fact, a history of injury to the back was less frequently elicited from the workers at Firbeck than at any other colliery. The possibility must also be considered that men in the wet seam may have had more heavy lifting to do. If this were so it might be expected that the " output per man/shift " would be greater in wet than in dry workings and in fact this was found to be the case at Firbeck. It is not, however, a universal finding in wet mines and may well at Firbeck have been due to other factors. It is known, for example, that roof conditions were more difficult in the dry workings and this would tend to reduce output. However caused, the increased output might of itself be sufficient to explain the more frequent radiological changes in those working at the wet face in this mine.

In the previous survey it was shown that the psychologically stable miners were more likely to show radiological change in the spine, due no doubt to their willingness to accept heavier tasks (Heron and Braithwaite, 1953), and it might be thought that such miners would be more likely also to accept work in a wet seam. This, however, is not supported by our findings. Both our psychometric and clinical assessments indicate that miners working in wet are less stable. This may, of course, be a result rather than a cause of accepting such work.

Air Velocity

It has not been found possible from our material to investigate the effect of air velocity either on incapacity or radiological changes as exposure to high air velocity is encountered only in the more restricted parts of the intake air-way where only a few haulage men, usually young lads not of an age to have disc changes, are employed. As, however, there is no increase of symptoms or radiological changes in the roadway workers as a whole, it would seem unlikely that work in high-velocity air currents is an important cause of disc change. It would be expected, of course, that a face worker might suffer no pain while in the relatively warm atmosphere of the face even though subjected to a degree of strain sufficient to cause appreciable damage to the intervertebral discs or ligaments, but on passing into the cold air the pain threshold would be lowered and the symptoms become apparent. The symptoms would thus be attributed by the victim to the cooling which immediately preceded their onset rather than to the earlier physical stress. Work in a cold current of air would, therefore, be intolerable to a man suffering from disc degeneration and result in loss of work unless a more suitable site could be found for him.

Knees

Apart from injury to the knee we have found no factor in mining which appears causally related to osteo-arthritis of the knee. A history of injury to the knee was obtained in 4% of miners, being greatest amongst roadway workers who also have most radiological change. Overt trauma accounts for only a few examples. As in the spine, the question of repeated minor injuries arises and is supported by the relatively low incidence of arthritis of the knee in the light manual and office workers who gave no history of overt trauma and probably suffered far less minor injury to the knee. The possibility that wet conditions may play a part in the symptomatology is suggested by the high incidence of incapacitating knee symptoms without increased radiological change at Firbeck. The fact that roadway workers in the mines have more osteo-arthritis of the knees than face workers should be interpreted with caution as it is likely that knee pain would be a frequent cause of transfer from the face to roadways.

SUMMARY

Factors responsible for the high incidence of intervertebral disc degeneration in miners have been investigated.

Comparison with dock workers has shown that disc degeneration is also severe in this heavy occupation but less so than in miners.

In both mining and other manual work there was a close relationship between the duration of heavy lifting and disc degeneration. Injuries to the back, whether blows or strains, were similarly related.

Of the miners, those working in wet conditions had more back-hip-sciatic pain and lost more work as a result. They also had more radiological changes of disc degeneration but these were less severe.

In miners there was a relationship between the position at work and spinal symptoms and incapacity. Those who stooped most were more severely affected. There was, however, no definite relationship between radiological changes and position at work, nor was there any very clear relationship between the duration of work in a stooping position and spinal symptoms or radiological changes. Personal factors, such as body height, length of back, and evidence of old rickets, were associated with a greater degree of incapacity but did not influence the severity of the radiological change.

Osteo-arthritis of the knees was found to be most frequent in underground roadway workers, less so in face workers, and still less in dockers and other manual workers. It was related to injury but not to kneeling, height of seam, distance walked, or heavy lifting. Though those working in wet showed more incapacity from knee symptoms, this was not increased by prolonged work in wet and the radiological changes were not affected. Radiological changes in the knees were related to body weight but symptoms and incapacity were unrelated. Deformity of the knees, on the other hand, affected symptoms and incapacity but not radiological changes.

Osteo-arthritis of the elbow, wrist, and hand were more frequent in miners than in other occupational groups.

I wish to thank Professors J. H. Kellgren and R. E. Lane and Dr. R. S. F. Schilling of the Departments of Rheumatism Research and Occupational Health of the University of Manchester for their generous help and guidance in carrying out this survey, also Mr. Nightingale and Dr. Waddell of the National Dock Labour Board and many members, and the staff of the N.C.B. and officials of the trades unions concerned. I am indebted to Miss N. Goodman for assistance in the statistical analysis.

Owing to lack of space it has been possible to include in this paper only a few of the Tables on which the conclusions have been based. The author will, however, be glad to supply further data to any who are interested and would care to write to him.

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APPENDIX

Unless the observer error in reading radiographs can be shown to be less than differences produced by occupational and environmental factors, doubt must inevitably be felt as to the validity of the results.

The radiographs were each read three times, once by each of two observers separately and once together. In the first half of the survey the individual readings preceded the combined reading (by some two years); in the second half they followed by one to two months. For the purpose of this study the radiological changes were divided into three grades: none, slight, and severe. The individual readings made by Observers 1 and 2 were of the same grade as the combined reading in 81% and 75% of instances respectively. Of the remainder some 12% were graded higher and 10% lower. In only 1% were the readings two grades out. As would be expected, agreement was closer in the second half of the survey.

In group results (Table A) the indications are that the maximum error is unlikely to be more than $\pm 11\%$. For the purpose of compiling the Tables in this paper a mean value calculated from the individual and combined readings has been used so avoiding the more marked observer differences. It follows that the radiological findings in this paper do not exactly correspond with those in our previous report based on the readings of one observer. In particular the use of the mean readings tends to reduce the proportion with no radiological changes as even two negative readings may be offset by a third high reading. The differences caused by this alternative method of expressing results are not however such as to alter the conclusions previously expressed, and the advantages of using the mean value undoubtedly outweigh the disadvantage of such slight discrepancies as may arise.

TABLE A
OBSERVER ERROR IN TOTAL READINGS OF SPINAL RADIOGRAPHS

386 Men	Severity			
	None	Slight	Severe	Not Known
Observer 1	76	176	134	—
Observer 2	83	152	151	—
Combined	70	186	129	1

The radiographs of the knees were similarly read to the same grade as the combined reading in 78 and 79% of cases respectively. In some 9% they were read as more severe and in 13% as less severe. The difference on individual readings is thus very similar in radiographs of spines and knees, but the error involved in reading groups was rather greater, being of the order of $\pm 20\%$ on the decision to classify the change as severe.

BOOK REVIEWS

Statistics of Industrial Rehabilitation (1955). *Ministry of Labour Gazette*, **63**, 121.

A recent issue of the *Ministry of Labour Gazette* features a review of figures relating to the Ministry's 15 industrial rehabilitation units. The Industrial Rehabilitation Scheme has been in existence since the first unit was set up at Egham in 1943 under the Disabled Persons (Employment) Act of 1944, and was rapidly expanded in 1948 to provide facilities for some 1,600 disabled persons. These courses are open to any person who may benefit, whether registered as disabled or not, on the recommendation of hospitals, family doctors, industrial medical officers, employment exchange officials, and others. The aim of the course is "to restore to the maximum degree of fitness for employment persons who, because of sickness, accident, or long unemployment, are in need of physical or mental toning up, and to give such of these persons as might need it, guidance as to the type of employment most likely to lead to their resettlement". Nearly 60,000 men and women have now passed through the units.

In this review, the Ministry attempts to throw some light on the degree of success achieved in different classes of disability, by an analysis of the last 500 cases terminating courses at each unit before June 30, 1952. Results are judged first on whether the subject was placed in employment or entered on a training course shortly after leaving an industrial rehabilitation unit and secondly on information from a follow-up inquiry.

One person in every six admitted to an industrial rehabilitation unit left before completing the course. These "premature terminations" have been excluded from analysis. Thus of the 7,000 cases under review, 83% completed the course, and of this 83%, 79% were placed in employment or admitted to training centres. Three thousand eight hundred and seventy-two of the original 5,801 persons completing the course replied to the follow-up questionnaire.

The analysis of medical categories shows no great variation in degree of successful resettlement between one medical group and another. The Ministry comments that this is no doubt due to the criterion of admission to the unit, namely, "Is this man (or woman) likely, after a short course of rehabilitation, to be fit for placing in industry or entry to a training centre?" This would appear to exclude the more severe cases of epilepsy or psychoneurosis, but "very few straight medical or orthopaedic cases would be refused admission". "Straight" cases are not defined and one wonders if they include compensation cases.

Premature terminations arise for a number of reasons. Medically, those in the psychosis groups have the highest number and mental defectives and cases of skin disease are low.

Training admissions following industrial rehabilitation courses show variations between medical categories, psychotics, bronchitics, and cardiac patients being among the least likely to be recommended for training, whereas patients with all forms of tuberculosis are judged good training prospects. Twenty per cent. of people completing the rehabilitation course were submitted to training.

Follow-up results six months after completing industrial rehabilitation courses show satisfactory resettlement in 85% of the "arthritis and rheumatism" groups and only 72% in diseases of the respiratory system (excluding tuberculosis). The latter figure is largely influenced by the seriously disabling nature of chronic bronchitis. The epileptic group had an initial placing figure of 70% but six months later this figure had fallen to less than 60% satisfactorily employed. Patients with organic nervous diseases are similarly disappointing even in the initial placing figure of 56%. G. FLETCHER

Principles of Medical Statistics, 6th ed. By A. Bradford Hill. (Pp. ix + 314. 10*s.* 6*d.*) London: The Lancet Ltd. 1955.

First published in 1937, this book will be known to medical research workers who use statistical methods in planning and interpreting results. This edition has a new chapter in which the special problems of clinical trials are clearly explained. There are also 16 pages of random sampling numbers with illustrations of how to use them. On comparing it with my 10-year-old third edition, dog-eared and dirty not, I hope, from abuse or neglect, there are important additions, such as a series of statistical exercises and, happily, the answers.

Professor Bradford Hill's book can best be introduced to those who do not know it by emphasizing that it is not written for the professional statistician but "for those who have to apply numerical methods of analysis to their records obtained in clinical and other branches of medicine". It is very suitable for industrial medical officers who have such excellent opportunities for keeping group records which can be used so profitably in the practice of preventive medicine.

This is a classic in medical literature probably because the author explains principles, encourages clear thinking with numbers, and gives some elementary lessons in "statistical tact" which is by no means always associated with the highest intelligence. RICHARD SCHILLING

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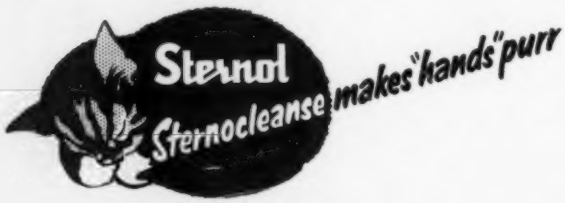

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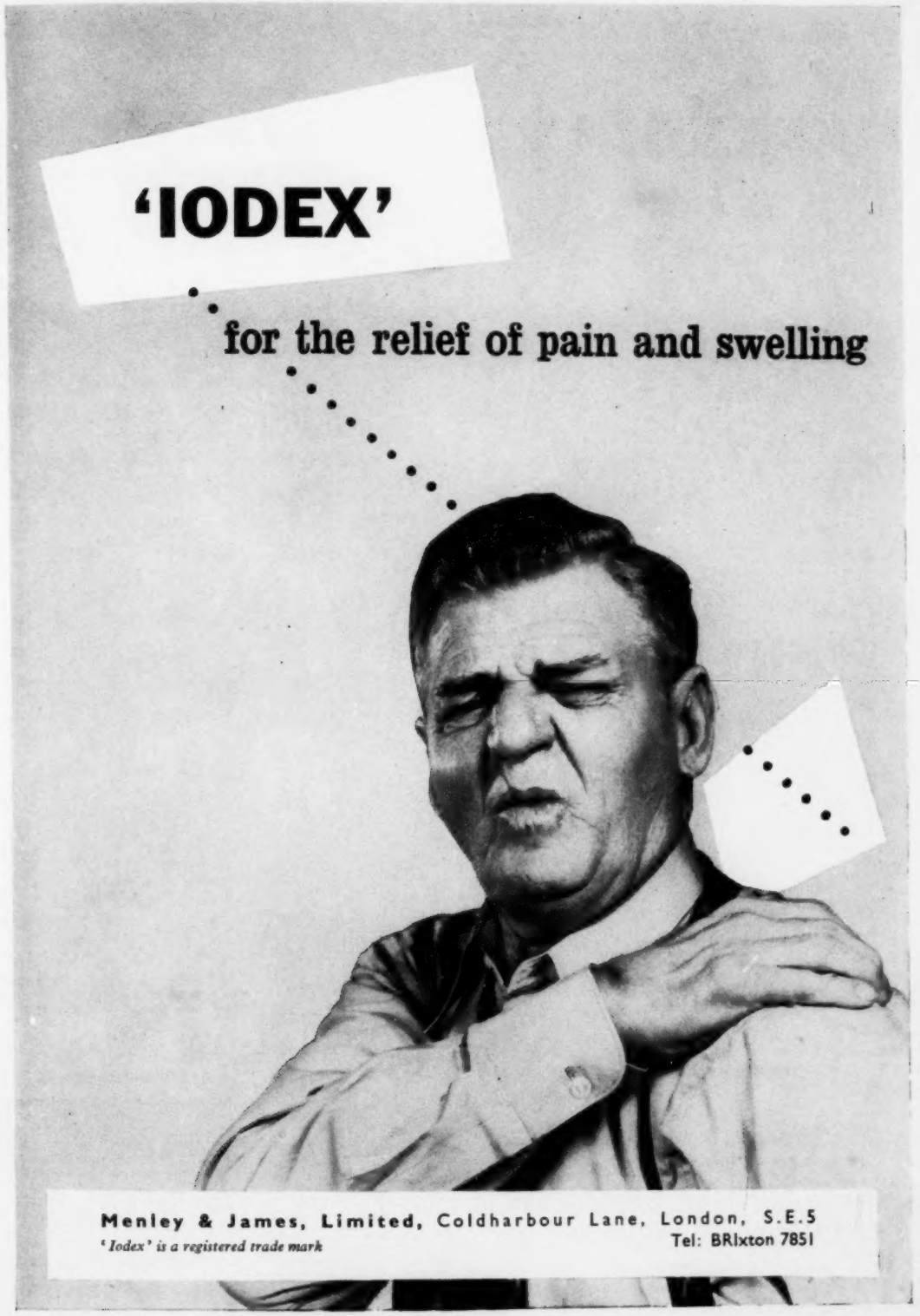
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